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NEWS 9 MAY 30 The F-Term thesaurus is now available in CA/CAplus
NEWS 10 JUN 02 The first reclassification of IPC codes now complete in
INPADOC
NEWS 11 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and
and display fields
NEWS 12 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
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NEWS 14 JUL 14 FSTA enhanced with Japanese patents
NEWS 15 JUL 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 16 AUG 09 INSPEC enhanced with 1898-1968 archive

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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STRUCTURE FILE UPDATES: 23 AUG 2006 HIGHEST RN 904004-64-4
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```
=> aryl (s) hydrocarbon (s) receptor (s) interacting (s) protein (s) like
      2437 ARYL
      1068 HYDROCARBON
      104391 RECEPTOR
      10326 INTERACTING
      4296564 PROTEIN
      78152 LIKE
L1          2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN
                  (S) LIKE
```

```
=> d ibib abs 11 1-2
'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
```

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

| | |
|--------|---|
| REG | - RN |
| SAM | - Index Name, MF, and structure - no RN |
| FIDE | - All substance data, except sequence data |
| IDE | - FIDE, but only 50 names |
| SQIDE | - IDE, plus sequence data |
| SQIDE3 | - Same as SQIDE, but 3-letter amino acid codes are used |
| SQD | - Protein sequence data, includes RN |
| SQD3 | - Same as SQD, but 3-letter amino acid codes are used |
| SQN | - Protein sequence name information, includes RN |
| CALC | - Table of calculated properties |
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| PROP | - EPROP and CALC |

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats

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ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PAT5 -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
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ENTER DISPLAY FORMAT (IDE):end

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FILE COVERS 1907 - 24 Aug 2006 VOL 145 ISS 9
FILE LAST UPDATED: 23 Aug 2006 (20060823/ED)

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=> 11

L2 2 L1

=> d ibib abs l2 1-2

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:978969 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 142:18187
TITLE: The status, quality, and expansion of the NIH
full-length cDNA project: The mammalian gene
collection (MGC)
AUTHOR(S): Gerhard, Daniela S.; Wagner, Lukas; Feingold, Elise
A.; Shenmen, Carolyn M.; Grouse, Lynette H.; Schuler,
Greg; Klein, Steven L.; Old, Susan; Rasooly, Rebekah;
Good, Peter; Guyer, Mark; Peck, Allicon M.; Derge,
Jeffery G.; Lipman, David; Collins, Francis S.
CORPORATE SOURCE: The MGC Project Team, NIH, USA
SOURCE: Genome Research (2004), 14(10b), 2121-2127
CODEN: GEREFS; ISSN: 1088-9051
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The National Institutes of Health's Mammalian Gene Collection (MGC)
project was designed to generate and sequence a publicly accessible cDNA
resource containing a complete open reading frame (ORF) for every human and
mouse gene. The project initially used a random strategy to select clones
from a large number of cDNA libraries from diverse tissues. Candidate clones
were chosen based on 5'-EST sequences, and then fully sequenced to high
accuracy and analyzed by algorithms developed for this project.
Currently, more than 11,000 human and 10,000 mouse genes are represented
in MGC by at least one clone with a full ORF. The random selection
approach is now reaching a saturation point, and a transition to protocols
targeted at the missing transcripts is now required to complete the mouse
and human collections. Comparison of the sequence of the MGC clones to
reference genome sequences reveals that most cDNA clones are of very high
sequence quality, although it is likely that some cDNAs may carry missense
variants as a consequence of exptl. artifact, such as PCR, cloning, or
reverse transcriptase errors. Recently, a rat cDNA component was added to
the project, and ongoing frog (*Xenopus*) and zebrafish (*Danio*) cDNA
projects were expanded to take advantage of the high-throughput MGC
pipeline. The sequence data for the full-length clones from this study
have been submitted to GenBank/EMBL/DDBJ under accession nos.
BC000001-BC077073. [This abstr record is one of 39 records for this
document necessitated by the large number of index entries required to fully
index the document and publication system constraints.].

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:55946 CAPLUS <<LOGINID::20060824>>

DOCUMENT NUMBER: 138:84320

TITLE: Generation and initial analysis of more than 15,000
full-length human and mouse cDNA sequences

AUTHOR(S): Strausberg, Robert L.; Feingold, Elise A.; Grouse,
Lynette H.; Derge, Jeffery G.; Klausner, Richard D.;
Collins, Francis S.; Wagner, Lukas; Shenmen, Carolyn
M.; Schuler, Gregory D.; Altschul, Stephen F.;
Zeeberg, Barry; Buetow, Kenneth H.; Schaefer, Carl F.;
Bhat, Narayan K.; Hopkins, Ralph F.; Jordan, Heather;
Moore, Troy; Max, Steve I.; Wang, Jun; Hsieh,
Florence; Diatchenko, Luda; Marusina, Kate; Farmer,
Andrew A.; Rubin, Gerald M.; Hong, Ling; Stapleton,

Mark; Soares, M. Bento; Bonaldo, Maria F.; Casavant, Tom L.; Scheetz, Todd E.; Brownstein, Michael J.; Usdin, Ted B.; Toshiyuki, Shiraki; Carninci, Piero; Prange, Christa; Raha, Sam S.; Loquellano, Naomi A.; Peters, Garrick J.; Abramson, Rick D.; Mullahy, Sara J.; Bosak, Stephanie A.; McEwan, Paul J.; McKernan, Kevin J.; Malek, Joel A.; Gunaratne, Preethi H.; Richards, Stephen; Worley, Kim C.; Hale, Sarah; Garcia, Angela M.; Gay, Laura J.; Hulyk, Stephen W.; Villalon, Debbie K.; Muzny, Donna M.; Sodergren, Erica J.; Lu, Xiuhua; Gibbs, Richard A.; Fahey, Jessica; Helton, Erin; Ketteman, Mark; Madan, Anuradha; Rodrigues, Stephanie; Sanchez, Amy; Whiting, Michelle; Madan, Anup; Young, Alice C.; Shevchenko, Yuriy; Bouffard, Gerard G.; Blakesley, Robert W.; Touchman, Jeffrey W.; Green, Eric D.; Dickson, Mark C.; Rodriguez, Alex C.; Grimwood, Jane; Schmutz, Jeremy; Myers, Richard M.; Butterfield, Yaron S. N.; Krzywinski, Martin I.; Skalska, Ursula; Smailus, Duane E.; Schnurch, Angelique; Schein, Jacqueline E.; Jones, Steven J. M.; Marra, Marco A.

CORPORATE SOURCE:

Mammalian Gene Collection (MGC) Program Team, National Cancer Institute, NIH, Bethesda, MD, 20892-2580, USA

SOURCE:

Proceedings of the National Academy of Sciences of the United States of America (2002), 99(26), 16899-16903

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER:

National Academy of Sciences

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The National Institutes of Health Mammalian Gene Collection (MGC) Program is a multiinstitutional effort to identify and sequence a cDNA clone containing a complete ORF for each human and mouse gene. ESTs were generated from libraries enriched for full-length cDNAs and analyzed to identify candidate full-ORF clones, which then were sequenced to high accuracy. The MGC has currently sequenced and verified the full ORF for a nonredundant set of >9000 human and >6000 mouse genes. Candidate full-ORF clones for an addnl. 7800 human and 3500 mouse genes also have been identified. All MGC sequences and clones are available without restriction through public databases and clone distribution networks. [This abstract record is one of eleven records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

=> AIPL1

L3 36 AIPL1

=> fil medline biosis caplus scisearch embase wpids

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=> AIP11

L4 268 AIP11

=> aryl (s) hydrocarbon (s) receptor (s) interacting (s) protein (s) like
L5 77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN
(S) LIKE

=> 14 and 15

L6 69 L4 AND L5

=> 14 or 15

L7 276 L4 OR L5

=> Trp278X and 17

L8 6 TRP278X AND L7

=> dup rem 18

PROCESSING COMPLETED FOR L8

L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

=> d ibib abs 19 1-3

L9 ANSWER 1 OF 3 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-416983 [39] WPIDS

DOC. NO. CPI: C2003-110372

TITLE: New aryl-hydrocarbon receptor
interacting protein-like 1 (AIP11) polynucleotides and proteins, useful for diagnosing or treating retinal diseases associated with AIP11 mutations, e.g. Leber congenital amaurosis.

DERWENT CLASS: B04 D16

INVENTOR(S): DAIGER, S P; SOHOCKI, M M

PATENT ASSIGNEE(S): (DAIG-I) DAIGER S P; (SOHO-I) SOHOCKI M M

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|--------------------|------|----|----|
| US 2003022165 | A1 | 20030130 (200339)* | | | 65 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| US 2003022165 | A1 | US 2001-765061 | 20010117 |

PRIORITY APPLN. INFO: US 2001-765061 20010117

AN 2003-416983 [39] WPIDS

AB US2003022165 A UPAB: 20030619

NOVELTY - A composition comprising a polynucleotide sequence, which comprises an aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1) sequence within the Leber congenital amaurosis 4 region of chromosome 17p13, and is a wild type or a mutant AIPL1 sequence.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a protein comprising any one of 7 amino acid sequences of 328-392 amino acids or variants of a sequence of 384 amino acids, or a polypeptide expressed by a polynucleotide comprising any one of 8 nucleotide sequences of 925-6689 bp or mutants of a sequence of 6689 base pairs (bp) that are selected from any one of 33 sequences consisting of 12-21 bp, all sequences fully defined in the specification;

(2) a purified polynucleotide sequence comprising any one of 71 fully defined sequences of 12-6689 bp given in the specification;

(3) a retinal disease diagnostic library comprising antisense DNA sequences, each sequence corresponding to a DNA sequence including a mutation of the aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1) gene consisting of any one of 33 fully defined sequences of 12-21 bp given in the specification, or their mixtures or combinations;

(4) a primer or probe comprising an AIPL1 sequence, which is a wild type or a mutant AIPL1 sequence, where the mutant AIPL1 contributes to a retinal disease;

(5) determining if an animal has a retinal disease or has a propensity to pass a retinal disease to offspring;

(6) a therapeutic method to treat retinal disease;

(7) determining if a patient has a mutant AIPL1 gene;

(8) producing a cell expressing an AIPL1 mutation;

(9) determining the presence of an AIPL1 mutant in a patient sample;

(10) a test kit for detecting AIPL1 mutations comprising a container containing at least one polynucleotide capable of hybridizing with a polynucleotide encoding at least one mutation consisting of Ala336 Delta 2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I, P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT-TGA), Val33ins 8 bp (GTGATCTT), Leu257del 9 bp (CTCCGGCAC), or their mixtures or combinations;

(11) screening compounds to determine their effectiveness in counteracting a cell's retinal behavior due to a mutation in its AIPL1 gene; and

(12) determining if a cell or sample has an AIPL1 mutation.

ACTIVITY - Ophthalmological. No biological data given.

MECHANISM OF ACTION - Gene Therapy; Ah Antagonist.

USE - The aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1) polynucleotides and proteins are useful for diagnosing or treating retinal diseases associated with AIPL1 mutations, e.g. Leber congenital amaurosis, juvenile retinitis pigmentosa, dominant cone-rod dystrophy, or other inherited or acquired retinopathies. The AIPL1 polynucleotides and proteins are also useful for determining if a cell or sample has an AIPL1 mutation, or if an animal has a retinal disease or has a propensity to pass a retinal disease to offspring. The methods are useful for screening of compounds that specifically binds to the mutated polypeptides, which can be used to treat resistant diseases that are associated with the mutations.

Dwg.0/10

L9 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001497731 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 11548141

TITLE: Leber's congenital amaurosis with anterior keratoconus in Pakistani families is caused by the Trp278X mutation in the AIPL1 gene on 17p.

AUTHOR: Damji K F; Sohocki M M; Khan R; Gupta S K; Rahim M; Loyer M; Hussein N; Karim N; Ladak S S; Jamal A; Bulman D; Koenekoop R K

CORPORATE SOURCE: Ottawa Hospital Research Institute, Ont..
kdamji@ottahospital.on.ca

SOURCE: Canadian journal of ophthalmology. Journal canadien d'ophtalmologie, (2001 Aug) Vol. 36, No. 5, pp. 252-9.
Journal code: 0045312. ISSN: 0008-4182.

PUB. COUNTRY: Canada

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200201

ENTRY DATE: Entered STN: 10 Sep 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 14 Jan 2002

AB BACKGROUND: Leber's congenital amaurosis (LCA) represents the earliest and severest form of retinal dystrophy leading to congenital blindness. A total of 20% of children attending blind schools have this disease. LCA has a multigenic basis and is proving central to our understanding of the development of the retina. We describe the clinical and molecular genetic features of four inbred pedigrees from neighbouring remote villages in northern Pakistan, in which some of the affected members have concurrent keratoconus. METHODS: History-taking and physical and eye examinations were performed in the field. Venipuncture, DNA extraction, studies of linkage to known LCA genes, automated sequencing and polymorphism analyses for haplotype assessments were done. RESULTS: We examined 12 affected and 15 unaffected family members. By history, there were an additional nine blind people in the four pedigrees. In each pedigree a consanguineous marriage was evident. We found a homozygous nonsense mutation in the AIPL1 gene, which replaces a tryptophan with a stop codon (Trp278X). The phenotype is severe and variable, despite the common molecular genetic etiology in each family. Affected patients had hand motion to no light perception vision and fundus findings ranging from maculopathy to diffuse pigmentary retinopathy. Three affected members had definite keratoconus, and two were suspects based on mild cone formation in the cornea of at least one eye. INTERPRETATION: We have identified four Pakistani families with a severe form of LCA that is associated with severe keratoconus in some affected members. The molecular etiology in all four families is a homozygous nonsense mutation, Trp278X, in the photoreceptor-pineal gene AIPL1. To our knowledge, this is one of the first phenotype-genotype correlations of AIPL1 -associated LCA.

L9 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 2000:488756 BIOSIS <>LOGINID::20060824>>

DOCUMENT NUMBER: PREV200000488877

TITLE: Leber Congenital Amaurosis with anterior keratoconus in Pakistani families is caused by the Trp278X mutation in the AIPL1 gene on 17p.

AUTHOR(S): Damji, K. F. [Reprint author]; Sohocki, M. M.; Khan, R.; Gupta, S. K. [Reprint author]; Rahim, M.; Loyer, M.; Hussein, N.; Karim, N.; Ladak, S. S.; Jamal, A.; Bulman, D. [Reprint author]; Koenekoop, R. K.

CORPORATE SOURCE: Ottawa Hospital Research Institute, Ottawa, ON, Canada

SOURCE: American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 382. print.
Meeting Info.: 50th Annual Meeting of the American Society

of Human Genetics. Philadelphia, Pennsylvania, USA. October 03-07, 2000. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002

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| | ENTRY | SESSION | |
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L1 FILE 'REGISTRY' ENTERED AT 18:56:18 ON 24 AUG 2006
2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L2 FILE 'CAPLUS' ENTERED AT 18:57:29 ON 24 AUG 2006
2 L1

L3 36 AIPL1

L4 FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
268 AIPL1
18:58:27 ON 24 AUG 2006
77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L5 69 L4 AND L5

L6 276 L4 OR L5

L7 6 TRP278X AND L7

L8 3 DUP REM L8 (3 DUPLICATES REMOVED)

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=> dup rem 16

| | | | |
|--|------------|---------|--|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| FULL ESTIMATED COST | 1.44 | 70.80 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| CA SUBSCRIBER PRICE | 0.00 | -1.50 | |

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FILE 'BIOSIS' ENTERED AT 19:15:47 ON 24 AUG 2006

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PROCESSING COMPLETED FOR L6
L10 33 DUP REM L6 (36 DUPLICATES REMOVED)

=> fil medline biosis caplus scisearch embase wpids
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SESSION
FULL ESTIMATED COST ENTRY 9.85 80.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
SESSION
CA SUBSCRIBER PRICE ENTRY 0.00 -1.50

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=> d ibib abs l10 1-33

L10 ANSWER 1 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:389493 BIOSIS <<LOGINID::20060824>>
DOCUMENT NUMBER: PREV200600400849
TITLE: The chaperone function of the LCA protein AIPL1 -
AIPL1 chaperone function.
AUTHOR(S): van der Spuy, Jacqueline [Reprint Author]; Cheetham,
Michael E.
CORPORATE SOURCE: UCL, Inst Ophthalmol, Div Pathol, London EC1V 9EL, UK
SOURCE: Hollyfield, JG [Editor]; Anderson, RE [Editor]; LaVail, MM
[Editor]. Adv. Exp. Med. Biol., (2006) pp. 471-476.
Advances in Experimental Medicine and Biology.
Publisher: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3,
D-14197 BERLIN, GERMANY. Series: ADVANCES IN EXPERIMENTAL
MEDICINE AND BIOLOGY.

Meeting Info.: 11th International Symposium on Retinal Degeneration. Perth, AUSTRALIA. August 23 -28, 2004. Fdn Fighting Blindness; Owings Mills.
CODEN: AEMBAP. ISSN: 0065-2598. ISBN: 0-387-28464-8(H).
DOCUMENT TYPE: Book; (Book Chapter)
Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Aug 2006
Last Updated on STN: 9 Aug 2006

L10 ANSWER 2 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:389442 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200600400798
TITLE: Biochemical function of the LCA linked protein,
aryl hydrocarbon receptor
interacting protein like-1 (AIPL1) - Role of AIPL1 in retina.
AUTHOR(S): Schwartz, Matthew L. [Reprint Author]; Hurley, James B.;
Ramamurthy, Visvanathan
CORPORATE SOURCE: Univ Washington, Dept Biochem, Seattle, WA 98195 USA
SOURCE: Hollyfield, JG [Editor]; Anderson, RE [Editor]; LaVail, MM [Editor]. Adv. Exp. Med. Biol., (2006) pp. 89-94. Advances in Experimental Medicine and Biology.
Publisher: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3, D-14197 BERLIN, GERMANY. Series: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY.
Meeting Info.: 11th International Symposium on Retinal Degeneration. Perth, AUSTRALIA. August 23 -28, 2004. Fdn Fighting Blindness; Owings Mills.
CODEN: AEMBAP. ISSN: 0065-2598. ISBN: 0-387-28464-8(H).
DOCUMENT TYPE: Book; (Book Chapter)
Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Aug 2006
Last Updated on STN: 9 Aug 2006

L10 ANSWER 3 OF 33 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006231633 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 16639031
TITLE: Effects of low AIPL1 expression on phototransduction in rods.
AUTHOR: Makino Clint L; Wen Xiao-Hong; Michaud Norman; Peshenko Igor V; Pawlyk Basil; Brush Richard S; Soloviev Maria; Liu Xiaoqing; Woodruff Michael L; Calvert Peter D; Savchenko Andrey B; Anderson Robert E; Fain Gordon L; Li Tiansen; Sandberg Michael A; Dizhoor Alexander M
CORPORATE SOURCE: Howe Laboratory, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary and Harvard Medical School, Boston 02114, USA.. cmakino@meei.harvard.edu
CONTRACT NUMBER: EY00871 (NEI)
EY014104 (NEI)
EY01844 (NEI)
EY04149 (NEI)
EY10309 (NEI)
EY11358 (NEI)
EY11522 (NEI)
EY12190 (NEI)
EY12944 (NEI)
SOURCE: Investigative ophthalmology & visual science, (2006 May Vol. 47, No. 5, pp. 2185-94.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 27 Apr 2006
Last Updated on STN: 7 Jun 2006
Entered Medline: 6 Jun 2006

AB PURPOSE: To investigate the impact of aryl hydrocarbon receptor-interacting protein-like (AIPL)-1 on photoreception in rods. METHODS: Photoresponses of mouse rods expressing lowered amounts of AIPL1 were studied by single-cell and electroretinogram (ERG) recordings. Phototransduction protein levels and enzymatic activities were determined in biochemical assays. Ca²⁺ dynamics were probed with a fluorescent dye. Comparisons were made to rods expressing mutant Y99C guanylate cyclase activating protein (GCAP)-1, to understand which effects arose from elevated dark levels of cGMP and Ca²⁺. RESULTS: Except for PDE, transduction protein levels were normal in low-AIPL1 retinas, as were guanylate cyclase (GC), rhodopsin kinase (RK), and normalized phosphodiesterase (PDE) activities. Y99C and low-AIPL1 rods were more sensitive to flashes than normal, but flash responses of low-AIPL1 rods showed an abnormal delay, reduced rate of increase, and longer recovery not present in Y99C rod responses. In addition, low-AIPL1 rods but not Y99C rods failed to reach the normal light-induced minimum in Ca²⁺ concentration. CONCLUSIONS: Reduced AIPL1 delayed the photoresponse, decreased its amplification constant, slowed a rate-limiting step in its recovery, and limited the light-induced decrease in Ca²⁺. Not all changes were attributable to decreased PDE or to elevated cGMP and Ca²⁺ in darkness. Therefore, AIPL1 directly or indirectly affects more than one component of phototransduction.

L10 ANSWER 4 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:399867 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200600392016
TITLE: Exclusion of LCA5 locus in a consanguineous Turkish family with macular coloboma-type LCA.
AUTHOR(S): Ozgul, R. K. [Reprint Author]; Bozkurt, B.; Kiratli, H.; Ogus, A.
CORPORATE SOURCE: Hacettepe Univ, Dept Biol Mol, Ankara, Turkey
rkozgul@hacettepe.edu.tr
SOURCE: Eye (Basingstoke), (JUL 2006) Vol. 20, No. 7, pp. 817-819.
ISSN: 0950-222X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Aug 2006
Last Updated on STN: 9 Aug 2006

AB Background Leber's congenital amaurosis (LCA) is an inherited retinal dystrophy, which causes severe visual impairment in early childhood. Recent molecular genetic studies have linked 11 loci (AIPL1, CRB1, CRX, GUCY2D, RPE65, RDH12, RPGRIP1, TULP1, LCA3, LCA5, and LCA9) to LCA. LCA5 is a new locus, which maps to the 6q11-q16 chromosomal region and was found to be associated with macular coloboma-type LCA in a Pakistani family. Herein, we describe the molecular genetic features of a consanguineous Turkish family in which four children have macular coloboma-type LCA. Methods Haplotype analysis was performed on the DNA of the family members using microsatellite markers against GUCY2D, RPE65, and LCA5. Genomic DNA was screened for mutations by means of single-strand conformational polymorphism (SSCP) analysis in exons of the RPE65 and CRX genes. Results In haplotype analysis, no linkage to LCA5 or GUCY2D loci was detected. None of the tested markers showed homozygosity or segregation between affected siblings. PCR-SSCP mutation analysis revealed no mutations in the screened RPE65 and CRX genes. Conclusion We excluded LCA5

as the genetic cause of macular coloboma-type LCA in this Turkish family. Macular coloboma-type LCA shows genetic heterogeneity and it is not possible to establish a phenotype-genotype correlation with LCA5 and macular coloboma.

L10 ANSWER 5 OF 33 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:366369 SCISEARCH <<LOGINID::20060824>>

THE GENUINE ARTICLE: BDY95

TITLE: Biochemical function of the LCA linked protein, aryl hydrocarbon receptor interacting protein like-1 (AIPL1) - Role of AIPL1 in retina

AUTHOR: Schwartz M L (Reprint); Hurley J B; Ramamurthy V

CORPORATE SOURCE: Univ Washington, Dept Biochem, Seattle, WA 98195 USA (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: RETINAL DEGENERATIVE DISEASES, (2006) Vol. 572, pp. 89-94.
ISSN: 0065-2598.

PUBLISHER: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3, D-14197
BERLIN, GERMANY.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 22

ENTRY DATE: Entered STN: 13 Apr 2006
Last Updated on STN: 19 Aug 2006

L10 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:671727 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:166667

TITLE: The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs

INVENTOR(S): Ueno, Yuki; Tsuda, Takanori; Takanori, Hitoshi; Yoshikawa, Toshikazu; Osawa, Toshihiko

PATENT ASSIGNEE(S): Biomarker Science Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 85 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2005198640 | A2 | 20050728 | JP 2004-53258 | 20040227 |
| PRIORITY APPLN. INFO.: | | | JP 2003-394758 | A 20031125 |

AB The curcuminoids- and anthocyanins-responsive gene expression profiles in adipocytes have been revealed. The curcuminoids- and anthocyanins-responsive genes are designed to be used as the index markers in the screenings of the substances that can affect the gene expression patterns in obesity and diabetes. These substances can be the candidates of anti-obesity and anti-diabetes drugs. Therefore, the groups of curcuminoids- and anthocyanins-responsive genes are intended to be used as markers in a form of kit such as DNA chip for the screening of anti-obesity and anti-diabetes drugs.

L10 ANSWER 7 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:44477 BIOSIS <<LOGINID::20060824>>
DOCUMENT NUMBER: PREV200600053678

TITLE: A screen for mutations of the Aipl1 gene in patients with supernormal scotopic Erg.

AUTHOR(S): Adams, S. M. [Reprint Author]; Weleber, R. G.; Berson, E. L.; Dryja, T. P.

SOURCE: IOVS, (2005) Vol. 46, No. Suppl. S, pp. 1820.

Meeting Info.: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology. Ft Lauderdale, FL, USA. May 01 -05, 2005. Assoc Res Vis & Ophthalmol.

CODEN: IOVSDA. ISSN: 0146-0404.

DOCUMENT TYPE: Conference; (Meeting)

Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jan 2006

Last Updated on STN: 4 Jan 2006

AB Purpose: The aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) is expressed specifically in adult rod photoreceptors where it is essential for photoreceptor viability and is one of the disease genes known to cause Leber congenital amaurosis. Mice homozygous with an AIPL1 hypomorphic mutation have a single. ash rod response with a higher amplitude and a greater time-to-peak than wild-type mice (Liu X et al. Proc Nat Acad Sci 2004; 101: 13903-8). We hypothesized that a hypomorphic mutation in this gene might be associated with a similar retinopathy in humans. To test this hypothesis, we screened the AIPL1 gene for mutations in patients with a supernormal scotopic ERG b-wave (Sandberg MA et al. Invest Ophthal Vis Sci 1990; 31: 2283-7).Methods: Leukocyte DNA samples from 8 unrelated patients with good acuity, lowrod responses to dim light and supernormal rod+ cone responses to bright white light. ashes were evaluated for mutations in all 6 coding exons and the flanking intron sequences by direct genomic sequencing. We also evaluated the DNA of relatives in 4 of the 8 probands. In total, 20 patients were screened.Results: One nonpathogenic missense change was found in 5 probands, Asp90His (GAC to CAC). This missense variant was found not to cosegregate with disease in one family. Three isocoding sequence substitutions were also found, Cys89Cys(TGC to TGT), Leu100Leu (CTA to CTG), and Pro217Pro (CCG to CCA). The missense change and the isocoding changes have been previously reported by other groups. Other variants identified were intronic, IVS1+36C>T, IVS1+45T>C, IVS2-10C>A, IVS4+48A>G, and IVS4-33T>C; which were all previously reported SNP's (<http://www.ncbi.nlm.nih.gov/>). All sequence variants were evaluated with splice-site prediction software and were predicted not to alter RNA splicing.Conclusions: We found no evidence for AIPL1 mutations as a cause of retinopathy in patients with supernormal scotopic ERGs.

L10 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:875831 CAPLUS <>LOGINID::20060824>>

DOCUMENT NUMBER: 143:264770

TITLE: Predominant rod photoreceptor degeneration in Leber congenital amaurosis

AUTHOR(S): van der Spuy, Jacqueline; Munro, Peter M. G.; Luthert, Philip J.; Preising, Markus N.; Bek, Toke; Heegaard, Steffen; Cheetham, Michael E.

CORPORATE SOURCE: Division of Pathology and Institute of Ophthalmology, University College London, London, UK

SOURCE: Molecular Vision (2005), 11, 542-553

CODEN: MVEPFB; ISSN: 1090-0535

URL: <http://www.molvis.org/molvis/v11/a64/v11a64-vander-spuy.pdf>

PUBLISHER: Molecular Vision

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB An unusual retinal vascular morphol. in an enucleated eye from a patient with Leber congenital amaurosis (LCA) has been associated with a mutation in AIPL1. The AIPL1 protein is expressed in the pineal

gland and retinal photoreceptors. In the retina, AIPL1 is expressed in both developing cone and rod photoreceptors, but it is restricted to rod photoreceptors in the adult human retina. Therefore, this study was conducted to determine the photoreceptor phenotype in this LCA patient to determine if photoreceptors were differentially affected. Addnl. genetic screening was performed and the consequences of the H82Y amino acid substitution characterized in an in vitro assay of NUB1 modulation. The morphol. of the photoreceptors was examined by light and electron microscopy. Immunohistochem. and immunofluorescent confocal microscopy was performed using a range of retinal photoreceptor markers. Transfection of the H82Y mutant AIPL1 in SK-N-SH cells revealed a normal subcellular localization and solubility but resulted in an increased ability of AIPL1 to redistribute GFP-NUB1 to the cytoplasm and resolve NUB1 fragment inclusion formation. Morphol., the LCA retina appeared to be cone-dominant with a single layer of cone-like cells remaining in the central retina. Photoreceptor outer segments were absent and the surviving residual inner segments were severely shortened. Severe degeneration of the LCA retina was associated with upregulation of glial fibrillary acidic protein (GFAP). No signal was detected for AIPL1, rhodopsin, or L/M and S cone opsins in the LCA retina. Double labeling with peanut agglutinin (PNA) and wheat germ agglutinin (WGA) supported a cone-dominant phenotype for the surviving photoreceptors in the LCA retina, as did double labeling for cone arrestin, and rod and cone recoverin. The cone arrestin signal was restricted to the residual photoreceptor inner segments and was not detected in the cell bodies, axons, or axon terminals of the surviving photoreceptors. Recoverin immunoreactivity was most intense in the residual photoreceptor inner segments. The phenotype in this patient suggests that although AIPL1 is required for the development of normal rod and cone photoreceptor function, it might only be essential for rod and not cone survival in the adult.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:420383 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 143:167734
TITLE: Dioxin: a review of its environmental effects and its aryl hydrocarbon receptor biology
AUTHOR(S): Mandal, Prabir K.
CORPORATE SOURCE: Department of Biology, University of North Florida, Jacksonville, FL, 32224, USA
SOURCE: Journal of Comparative Physiology, B: Biochemical, Systemic, and Environmental Physiology (2005), 175(4), 221-230
CODEN: JPBPD; ISSN: 0174-1578
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. A highly persistent trace environmental contaminant and one of the most potent toxicants known is dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin or TCDD). TCDD induces a broad spectrum of biol. responses, including induction of cytochrome P 450 1A1 (CYP1A1), disruption of normal hormone signalling pathways, reproductive and developmental defects, immunotoxicity, liver damage, wasting syndrome, and cancer. Its classification was upgraded from "possible human carcinogen" (group 2B) to "human carcinogen" (group 1) by the International Agency for Research on Cancer (IARC) in 1997. Exposure to TCDD may also cause changes in sex ratio, and tumor promotion in other animals. Because of the growing public and scientific concern, toxicol. studies were initiated to analyze the short- and long-term effects of dioxin. TCDD brings about a wide variety of toxic and biochem. effects via aryl hydrocarbon receptor

(AhR)-mediated signaling pathways. Essential steps in this adaptive mechanism include AhR binding of ligand in the cytoplasm of cells associated with 2 mols. of chaperone heatshock protein (Hsp90) and AhR interactive protein, translocation of the receptor to the nucleus, dimerization with the Ah receptor nuclear translocator, and binding of this heterodimeric transcription factor (present in CYP1A) to dioxin-responsive elements upstream of promoters that regulate the expression of genes involved in xenobiotic metabolism

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 33 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004559105 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 15347646
TITLE: The Leber congenital amaurosis protein AIPL1 modulates the nuclear translocation of NUB1 and suppresses inclusion formation by NUB1 fragments.
AUTHOR: van der Spuy Jacqueline; Cheetham Michael E
CORPORATE SOURCE: Division of Pathology, Institute of Ophthalmology, University College London, London, EC1V 9EL, United Kingdom.
SOURCE: The Journal of biological chemistry, (2004 Nov 12) Vol. 279, No. 46, pp. 48038-47. Electronic Publication: 2004-08-30. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 9 Nov 2004
Last Updated on STN: 22 Jan 2005
Entered Medline: 21 Jan 2005

AB Mutations in the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) cause the blinding disease Leber congenital amaurosis (LCA). The similarity of AIPL1 to AIP has led to suggestions that AIPL1 could function in a similar manner to AIP in facilitating protein translocation and as a component of chaperone complexes. AIPL1 interacts with the cell cycle regulator NEDD8 ultimate buster protein 1 (NUB1). As AIPL1 is predominantly cytoplasmic and NUB1 is predominantly nuclear, we tested the hypothesis that AIPL1 could modulate the nuclear translocation of NUB1. Co-transfection of AIPL1 with GFP-NUB1 resulted in a shift of GFP-NUB1 subcellular distribution toward the cytoplasm. Interestingly, AIPL1 was able to act in a chaperone-like fashion to efficiently suppress inclusion formation by NUB1 fragments. Co-transfection of AIPL1 with GFP-NUB1-N and GFP-NUB1-C resulted in an AIPL1-dependent suppression of GFP-NUB1-N perinuclear inclusions and GFP-NUB1-C intranuclear inclusions leading to the redistribution of these fragments in the cytoplasm. This chaperone-like function of AIPL1 was specific for NUB1, since AIPL1 was unable to suppress the inclusion formation by unrelated aggregation-prone proteins and AIP had no effect on NUB1 localization or inclusion formation. We examined the effect of a range of pathogenic and engineered mutations on the ability of AIPL1 to modulate NUB1 localization or inclusion formation. With the exception of W278X, which formed non-functional SDS-insoluble inclusions, all of the pathogenic mutations studied were soluble and could modulate NUB1 with varying efficiency compared with the wild-type protein. The effect of AIPL1 on NUB1 required the C-terminal region of AIPL1, as engineered C-terminal truncation mutations had no effect on NUB1. These data show that AIPL1 can modulate protein

translocation and act in a chaperone-like manner and suggest that AIPL1 is an important modulator of NUB1 cellular function.

L10 ANSWER 11 OF 33 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004473023 MEDLINE <> LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 15365173
TITLE: AIPL1, the protein that is defective in Leber congenital amaurosis, is essential for the biosynthesis of retinal rod cGMP phosphodiesterase.
AUTHOR: Liu Xiaoqing; Bulgakov Oleg V; Wen Xiao-Hong; Woodruff Michael L; Pawlyk Basil; Yang Jun; Fain Gordon L; Sandberg Michael A; Makino Clint L; Li Tiansen
CORPORATE SOURCE: Berman-Gund Laboratory for the Study of Retinal Degenerations, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA 02114, USA.
CONTRACT NUMBER: EY01844 (NEI)
EY10309 (NEI)
EY11358 (NEI)
EY14104 (NEI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2004 Sep 21) Vol. 101, No. 38, pp. 13903-8. Electronic Publication: 2004-09-13. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 23 Sep 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 3 Dec 2004

AB Aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) is a member of the FK-506-binding protein family expressed specifically in retinal photoreceptors. Mutations in AIPL1 cause Leber congenital amaurosis, a severe early-onset retinopathy that leads to visual impairment in infants. Here we show that knockdown of AIPL1 expression in mice also produces a retinopathy but over a more extended time course. Before any noticeable pathology, there was a reduction in the level of rod cGMP phosphodiesterase (PDE) proportional to the decrease in AIPL1 expression, whereas other photoreceptor proteins were unaffected. Consistent with less PDE in rods, flash responses had a delayed onset, a reduced gain, and a slower recovery of flash responses. We suggest that AIPL1 is a specialized chaperone required for rod PDE biosynthesis. Thus loss of AIPL1 would result in a condition that phenocopies retinal degenerations in the rd mouse and in a subgroup of human patients.

L10 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:808380 CAPLUS <> LOGINID::20060824>>
DOCUMENT NUMBER: 141:330027
TITLE: Leber congenital amaurosis linked to AIPL1: A mouse model reveals destabilization of cGMP phosphodiesterase
AUTHOR(S): Ramamurthy, Visvanathan; Niemi, Gregory A.; Reh, Thomas A.; Hurley, James B.
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2004), 101(38), 13897-13902
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Leber congenital amaurosis (LCA4) has been linked to mutations in the photoreceptor-specific gene Aryl hydrocarbon interacting protein like 1 (Aip1l). To investigate the essential role of AIPL1 in retina, the authors generated a mouse model of LCA by inactivating the Aip1l gene. In Aip1l^{-/-} retinas, the outer nuclear layer develops normally, but rods and cones then quickly degenerate. Aip1l^{-/-} mice have highly disorganized, short, fragmented photoreceptor outer segments and lack both rod and cone electroretinogram responses. Recent biochem. evidence indicates that AIPL1 can enhance protein farnesylation. The authors' study reveals that rod cGMP phosphodiesterase, a farnesylated protein, is absent and cGMP levels are elevated in AIPL1^{-/-} retinas before the onset of degeneration. The authors' findings demonstrate that AIPL1 enhances the stability of phosphodiesterase and is essential for photoreceptor viability.

REFERENCE COUNT:

30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 33 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004369718 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 15249368
TITLE: The phenotype of Leber congenital amaurosis in patients with AIPL1 mutations.
AUTHOR: Dharmaraj Sharola; Leroy Bart P; Schecki Melanie M; Koenekoop Robert K; Perrault Isabelle; Anwar Khalid; Khalil Shagufta; Devi R Summathi; Birch David G; De Pool Elaine; Izquierdo Natalio; Van Maldergem Lionel; Ismail Mohammad; Payne Annette M; Holder Graham E; Bhattacharya Shomi S; Bird Alan C; Kaplan Josseline; Maumenee Irene H
CORPORATE SOURCE: Johns Hopkins Center for Hereditary Eye Diseases, Wilmer Eye Institute, Johns Hopkins Medical Institutions, Baltimore, MD 21287-9237, USA.. sdharmaraj@jhmi.edu
SOURCE: Archives of ophthalmology, (2004 Jul) Vol. 122, No. 7, pp. 1029-37.
Journal code: 7706534. ISSN: 0003-9950.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 28 Jul 2004
Last Updated on STN: 7 Aug 2004
Entered Medline: 6 Aug 2004

AB OBJECTIVES: To describe the phenotype of Leber congenital amaurosis (LCA) in 26 probands with mutations in aryl hydrocarbon receptor interacting protein-like 1 protein (AIPL1) and compare it with phenotypes of other LCA-related genes. To describe the electroretinogram (ERG) in heterozygote carriers. METHODS: Patients with AIPL1-related LCA were identified in a cohort of 303 patients with LCA by polymerase chain reaction single-strand confirmational polymorphism mutation screening and/or direct sequencing. Phenotypic characterization included clinical and ERG evaluation. Seven heterozygous carrier parents also underwent ERG testing. RESULTS: Seventeen homozygotes and 9 compound heterozygotes were identified. The W278X mutation was most frequent (48% of alleles). Visual acuities ranged from light perception to 20/400. Variable retinal appearances, ranging from near normal to varying degrees of chorioretinal atrophy and intraretinal pigment migration, were noted. Atrophic and/or pigmentary macular changes were present in 16 (80%) of 20 probands. Keratoconus and cataracts were identified in 5 (26%) of 19 patients, all

of whom were homozygotes. The ERG of a parent heterozygote carrier revealed significantly reduced rod function, while ERGs for 6 other carrier parents were normal. CONCLUSIONS: The phenotype of LCA in patients with AIPL1 mutations is relatively severe, with a maculopathy in most patients and keratoconus and cataract in a large subset. Rod ERG abnormalities may be present in heterozygous carriers of AIPL1 mutations. CLINICAL RELEVANCE: Understanding and recognizing the phenotype of LCA may help in defining the course and severity of the disease. Identifying the gene defect is the first step in preparation for therapy since molecular diagnosis in LCA will mandate the choice of treatment.

L10 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2004:309237 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 140:337231
TITLE: Abolished interaction of NUB1 with mutant
AIPL1 involved in Leber congenital amaurosis
AUTHOR(S): Kanaya, Koichi; Sohocki, Melanie M.; Kamitani, Tetsu
CORPORATE SOURCE: Medical School, Department of Internal Medicine, The
University of Texas-Houston Health Science Center,
Houston, TX, 77030, USA
SOURCE: Biochemical and Biophysical Research Communications
(2004), 317(3), 768-773
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leber congenital amaurosis (LCA) is often considered the most severe
inherited retinopathy, and AIPL1 was the fourth gene identified
as associated with LCA. Although the function of AIPL1 is unknown,
it has been reported to interact with NUB1. Here, the authors searched
for a NUB1-binding site on AIPL1 and located it between amino
acid residues 181 and 330 in AIPL1. Importantly, many
LCA-associated mutations of AIPL1 have been found at this site.
Hence, the authors hypothesized that the interaction between NUB1 and
AIPL1 is affected in patients with LCA. To test this possibility,
the authors used three different assays to investigate the interaction
between NUB1 and the AIPL1 mutants associated with LCA. Some of
the AIPL1 mutants did not interact with NUB1, suggesting that
abolishment of this interaction is involved in the pathogenesis of LCA.
Other AIPL1 mutants, however, did interact with NUB1, suggesting
that other mols. are also involved in the pathogenesis.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 33 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004368026 MEDLINE <<LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 15270697
TITLE: Role of AIP and its homologue the blindness-associated
protein AIPL1 in regulating client protein
nuclear translocation.
AUTHOR: van der Spuy J; Cheetham M E
CORPORATE SOURCE: Division of Pathology, Institute of Ophthalmology,
University College London, 11-43 Bath Street, London EC1V
9EL, UK.. j.spuy@ucl.ac.uk
SOURCE: Biochemical Society transactions, (2004 Aug) Vol. 32, No.
Pt 4, pp. 643-5.
Journal code: 7506897. ISSN: 0300-5127.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 25 Jul 2004
Last Updated on STN: 16 Mar 2005
Entered Medline: 15 Mar 2005

AB Mutations in the AIPL1 (aryl hydrocarbon receptor interacting protein-like 1) cause the blinding disease Leber's congenital amaurosis. AIPL1 is a homologue of the AIP. AIP functions as part of a chaperone heterocomplex to facilitate signalling by the AhR and plays an important role in regulating the nuclear translocation of the receptor. We review the evidence for the role of AIP in protein translocation and compare the potential functions of AIPL1 in the translocation of its interacting partner the NEDD8 ultimate buster protein 1.

L10 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:375810 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 141:121675
TITLE: Leber congenital amaurosis: Comprehensive survey of the genetic heterogeneity, refinement of the clinical definition, and genotype-phenotype correlations as a strategy for molecular diagnosis
AUTHOR(S): Hanein, Sylvain; Perrault, Isabelle; Gerber, Sylvie; Tanguy, Gaelle; Barbet, Fabienne; Ducrocq, Dominique; Calvas, Patrick; Dollfus, Helene; Hamel, Christian; Lopponen, Tuija; Munier, Francis; Santos, Louisa; Shalev, Stavit; Zafeiriou, Dimitrios; Dufier, Jean-Louis; Munnich, Arnold; Rozet, Jean-Michel; Kaplan, Josseline
CORPORATE SOURCE: Unite de Recherches sur les Handicaps Genetiques de l'Enfant, Hopital Necker - Enfants Malades, Paris, Fr.
SOURCE: Human Mutation (2004), 23(4), 306-317
CODEN: HUMUE3; ISSN: 1059-7794
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is the earliest and most severe form of all inherited retinal dystrophies, responsible for congenital blindness. Disease-associated mutations have been hitherto reported in seven genes. These genes are all expressed preferentially in the photoreceptor cells or the retinal pigment epithelium but they are involved in strikingly different physiol. pathways resulting in an unforeseeable physiopathol. variety. This wide genetic and physiol. heterogeneity that could largely increase in the coming years, hinders the mol. diagnosis in LCA patients. The genotyping is, however, required to establish genetically defined subgroups of patients ready for therapy. Here, the authors report a comprehensive mutational anal. of the all known genes in 179 unrelated LCA patients, including 52 familial and 127 sporadic (27/127 consanguineous) cases. Mutations were identified in 47.5% patients. GUCY2D appeared to account for most LCA cases of our series (21.2%), followed by CRB1 (10%), RPE65 (6.1%), RPGRIP1 (4.5%), AIPL1 (3.4%), TULP1 (1.7%), and CRX (0.6%). The clin. history of all patients with mutations was carefully revisited to search for phenotype variations. Sound genotype-phenotype correlations were found that allowed patients to be divided into two main groups. The first one includes patients whose symptoms fit the traditional definition of LCA, i.e., congenital or very early cone-rod dystrophy, while the second group gathers patients affected with severe yet progressive rod-cone dystrophy. Besides, objective ophthalmol. data allowed each group to be subdivided into two subtypes. Based on these findings, the authors have drawn decisional flowcharts directing the mol. anal. of LCA genes in a given case. These flowcharts will hopefully lighten the heavy task of genotyping new patients but only if one has access to the most precise clin. history since birth.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2004:1047682 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 142:72707
TITLE: Retinal degeneration in Aip1l-deficient mice: a new genetic model of Leber congenital amaurosis
AUTHOR(S): Dyer, Michael A.; Donovan, Stacy L.; Zhang, Jiakun; Gray, Jonathan; Ortiz, Angelica; Tenney, Rebeca; Kong, Jian; Allikmets, Rando; Sohocki, Melanie M.
CORPORATE SOURCE: Department of Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA
SOURCE: Molecular Brain Research (2004), 132(2), 208-220
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is the most severe inherited retinopathy, with the earliest age of onset. Because this currently incurable disease is present from birth and is a relatively rare disorder, the development of animal models that closely resemble the phenotype in patients is especially important. The authors' previous genetic analyses of LCA patients identified mutations in the aryl-hydrocarbon interacting protein-like 1 (AIPL1) gene. Here they present the development of an animal model of AIPL1-associated LCA, the Aip1l-deficient mouse. Aip1l is expressed at low levels throughout human and mouse retinal development and is rapidly upregulated as photoreceptors differentiate. The mouse displays rapid retinal degeneration and massive Mueller cell gliosis, resembling the phenotype of the rd mouse, which is caused by a mutation in the gene for the β -subunit of the rod-specific phosphodiesterase. The authors confirm that this phenotype is consistent with the human disease using electroretinograms, and document the disease pathogenesis by analyzing the development of all retinal cell types and synaptogenesis during retinal histogenesis. Ectopic expression of AIPL1 led to deregulated retinal progenitor cell proliferation and alterations in cell fate specification; however, no gross abnormalities of proliferation during retinal development were detected. Data from anal. of proliferation and cell fate specification during retinal development of Aip1l-deficient mice suggests that there may be redundancy or compensation for Aip1l loss by other related proteins. Because this mouse model closely mimics the human retinopathy caused by homozygous mutations in this gene, it provides a preclin. model for testing therapies to rescue the vision of children whose blindness is caused by AIPL1 mutations.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2003:77413 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 138:135203
TITLE: Mutations in the AIPL1 gene encoding an aryl receptor interacting protein homolog on chromosome 17p cause Leber congenital amaurosis 4
INVENTOR(S): Sohocki, Melanie M.; Daiger, Stephen P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 65 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 2003022165 | A1 | 20030130 | US 2001-765061 | 20010117 |
| PRIORITY APPLN. INFO.: | | | US 2001-765061 | 20010117 |

AB A gene expressed in the eye and pineal gland encoding an aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1) and that appears to play a role in the etiol. of Leber congenital amaurosis is mapped and cloned and mutant alleles characterized. Leber congenital amaurosis (LCA) is the most severe form of inherited retinal dystrophy and the most frequent cause of inherited blindness in children. LCA is usually inherited in an autosomal recessive fashion, although rare dominant cases have been reported. One form of LCA, LCA4, maps to chromosome 17p13 and is genetically distinct from other forms of LCA. The inventors recently identified the gene associated with LCA4, AIPL1 (aryl-hydrocarbon receptor interacting protein-like 1) and identified three mutations that were the cause of blindness in five families with LCA. Identification of the role of the gene was by cloning and mapping and by pedigree studies.

L10 ANSWER 19 OF 33 MEDLINE on STN DUPLICATE 9
 ACCESSION NUMBER: 2003507278 MEDLINE <>LOGINID::20060824>>
 DOCUMENT NUMBER: PubMed ID: 14555765
 TITLE: AIPL1, a protein implicated in Leber's congenital amaurosis, interacts with and aids in processing of farnesylated proteins.
 AUTHOR: Ramamurthy Visvanathan; Roberts Melanie; van den Akker Focco; Niemi Gregory; Reh T A; Hurley James B
 CORPORATE SOURCE: Departments of Biochemistry and Biological Structure, University of Washington, Seattle, WA 98195, USA.
 CONTRACT NUMBER: EY 013572-01 (NEI)
 NS 28308-14 (NINDS)
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Oct 28) Vol. 100, No. 22, pp. 12630-5. Electronic Publication: 2003-10-10.
 Journal code: 7505876. ISSN: 0027-8424.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200401
 ENTRY DATE: Entered STN: 30 Oct 2003
 Last Updated on STN: 6 Jan 2004
 Entered Medline: 5 Jan 2004

AB The most common form of blindness at birth, Leber's congenital amaurosis (LCA), is inherited in an autosomal recessive fashion. Mutations in six different retina-specific genes, including a recently discovered gene, AIPL1, have been linked to LCA in humans. To understand the molecular basis of LCA caused by aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) mutations, and to elucidate the normal function of AIPL1, we performed a yeast two-hybrid screen using AIPL1 as bait. The screen demonstrated that AIPL1 interacts specifically with farnesylated proteins. Mutations in AIPL1 linked to LCA compromise this activity. These findings suggest that the essential function of AIPL1 within photoreceptors requires interactions with farnesylated proteins. Analysis of isoprenylation in cultured human cells shows that AIPL1 enhances the processing of farnesylated proteins. Based on these findings, we propose that AIPL1 interacts with farnesylated proteins and plays an essential

role in processing of farnesylated proteins in retina.

L10 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:881235 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 140:161686
TITLE: Analysis of three genes in Leber congenital amaurosis
in Indonesian patients
AUTHOR(S): Sitorus, Rita S.; Lorenz, Birgit; Preising, Markus N.
CORPORATE SOURCE: Department of Paediatric Ophthalmology, Strabismology
and Ophthalmogenetics, klinikum, University of
Regensburg, Regensburg, 93053, Germany
SOURCE: Vision Research (2003), 43(28), 3087-3093
CODEN: VISRAM; ISSN: 0042-6989
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose. To assess the frequency, the pattern of disease causing mutations, and phenotypic variations in patients with Leber congenital amaurosis (LCA) from Indonesia. Patients and methods. Twenty-one unrelated index cases with a clin. diagnosis of LCA were screened for mutations in the coding sequence of RetGC1, RPE65 and AIPL1 gene with single strand conformation polymorphism anal. followed by direct sequencing and restriction enzyme digestion. Results. Four novel disease causing mutations were identified: Three in the RPE65 gene (106del9bp, G32V and Y435C) in two of 21 index cases and one in the AIPL1 (K14E). Two of them were homozygous and one was compound-heterozygous. No disease causing mutation was identified in RetGC1. Conclusions. The four novel disease causing mutations identified in this study confirmed the diagnosis of LCA which has not been recognized before in Indonesia. The frequency of RPE65 mutations was 9.5%; and of AIPL1 mutations 4.8%. This was in general accordance with previous studies reported from other countries. Unlike in those studies, no disease causing RetGC1 mutations could be identified in the authors' patients. Phenotypically, the RPE65 and AIPL1 mutations identified in this study caused nearly total blindness by the second decade of life, but had a different onset of symptoms. The patients with the RPE65 mutations retained some useful visual function until the end of the first decade, which progressed to total blindness during the second decade of life, whereas the (homozygous) AIPL1 mutation was associated with nearly total blindness from infancy on. Therefore, RPE65 mutations have to be considered to cause early onset severe retinal degeneration (EOSRD), and AIPL1 mutations a form of LCA.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:204282 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 140:37579
TITLE: The inherited blindness associated protein AIPL1 interacts with the cell cycle regulator protein NUB1. [Erratum to document cited in CA138:118994]
AUTHOR(S): Akey, Dayna T.; Zhu, Xuemei; Dyer, Michael; Li, Aimin; Sorensen, Adam; Blackshaw, Seth; Fukuda-Kamitani, Taeko; Daiger, Stephen P.; Craft, Cheryl M.; Kamitani, Tetsu; Sohocki, Melanie M.
CORPORATE SOURCE: Department of Environmental Health, Center for Genome Information, University of Cincinnati, Cincinnati, OH, 45267, USA
SOURCE: Human Molecular Genetics (2003), 12(4), 451
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Figure 4, the left blot was transposed; the corrected figure is given.

L10 ANSWER 22 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004001184 EMBASE <>LOGINID::20060824>>
TITLE: Gene therapy for leber congenital amaurosis.
AUTHOR: Dejneka N.S.; Surace E.M.; Bennett J.
CORPORATE SOURCE: United States. ndejneka@mail.med.upenn.edu
SOURCE: Advances in Experimental Medicine and Biology, (2003) Vol. 533, pp. 415-422. .
Refs: 61
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
012 Ophthalmology
022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2004
Last Updated on STN: 16 Jan 2004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L10 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:647291 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 142:275624
TITLE: Functional studies of AIPL1: potential role of AIPL1 in cell cycle exit and/or differentiation of photoreceptors
AUTHOR(S): Akey, Dayna T.; Zhu, Xuemei; Dyer, Michael; Li, Amin; Sorensen, Adam; Fukada-Kamitani, Taeko; Daiger, Stephen P.; Craft, Cheryl; Kamitani, Tetsu; Sohocki, Melanie M.
CORPORATE SOURCE: University of Cincinnati, Cincinnati, OH, 45267, USA
SOURCE: Advances in Experimental Medicine and Biology (2003), 533(Retinal Degenerations), 287-295
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aryl hydrocarbon receptor interacting protein-like 1 (AIPL1)
plays a role in cytosolic stability and/or nuclear transport of NUB1 during regulation of cell cycle progression during photoreceptor development. This function would be consistent with the severe, early-onset blindness observed in patients with Leber congenital amaurosis caused by mutations of AIPL1. It was shown that co-immunopptn. expts. in cells of retinal origin that AIPL1 specifically interacts with a 50 kDa NUB1 protein, which is 16 kDa smaller than that present in other tissues.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 33 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:998991 SCISEARCH <>LOGINID::20060824>>
THE GENUINE ARTICLE: 709CK
TITLE: Molecular basis of Leber congenital amaurosis caused by mutations in aryl hydrocarbon receptor interacting protein like-1 (AIPL1)

AUTHOR: Ramamurthy V (Reprint); van den Akker F; Hurley J
CORPORATE SOURCE: Univ Washington, Dept Biochem, Seattle, WA 98195 USA;
Cleveland Clin Fdn, Lerner Res Inst, Dept Mol Biol, NB20,
Cleveland, OH 44195 USA; Cleveland Clin Fdn, Lerner Res
Inst, Ctr Struct Biol, Cleveland, OH 44195 USA.
COUNTRY OF AUTHOR: USA
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (MAY 2003)
Vol. 44, Supp. [2], pp. U276-U276. MA 3554.
ISSN: 0146-0404.
PUBLISHER: ASSOC RESEARCH VISION OPHTHALMOLOGY INC, 12300 TWINBROOK
PARKWAY, ROCKVILLE, MD 20852-1606 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 8 Dec 2003
Last Updated on STN: 8 Dec 2003

L10 ANSWER 25 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN
ACCESSION NUMBER: 2003:554155 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200300551430
TITLE: MOLECULAR BASIS OF LEBER CONGENITAL AMAUROSIS CAUSED BY
MUTATIONS IN ARYL HYDROCARBON
RECEPTOR INTERACTING PROTEIN
LIKE - 1 (AIPL1).
AUTHOR(S): Ramamurthy, V. [Reprint Author]; Van Den Akker, F.; Hurley,
J. [Reprint Author]
CORPORATE SOURCE: Biochemistry Department, University of Washington, Seattle,
WA, USA
SOURCE: ARVO Annual Meeting Abstract Search and Program Planner,
(2003) Vol. 2003, pp. Abstract No. 3554. cd-rom.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale, FL,
USA. May 04-08, 2003. Association for Research in Vision
and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Nov 2003
Last Updated on STN: 26 Nov 2003

AB Purpose: Leber's congenital amaurosis (LCA) is the most common form of inherited blindness at birth. LCA is usually inherited in autosomal recessive fashion. Mutations in six different retina specific genes have been linked to LCA in humans. Recently, several mutations in a novel gene, AIPL1, have been linked to LCA. The aim of this study is to understand the molecular basis of LCA caused by mutations in AIPL1 and to elucidate the normal function of AIPL1.
Methods: Proteins that interact with AIPL1 were isolated by yeast-two hybrid analysis using human AIPL1 as bait and bovine retinal cDNA prey library. The interaction was further confirmed using in vitro binding assay. Proteins that were isolated by yeast two hybrid analysis were also tested for their ability to interact with various homozygous mutants in AIPL1 that are linked to LCA in humans.
Results: Of approximately 2.5 x 10⁶ colonies screened, we identified 34 clones that interacted with AIPL1. These 34 clones represent 8 different proteins. Six of the eight AIPL1 targets (32 clones) identified by the screen encode proteins with a C-terminal prenylation motif. Both our yeast two hybrid analysis and in vitro binding studies confirm that AIPL1 specifically interacts with farnesylated proteins. Homozygous mutations in AIPL1 linked to LCA prevent AIPL1 from interacting with farnesylated proteins.
Conclusions: Our study identified a biochemical activity of AIPL1

that is linked to LCA. This study defines a novel interaction between AIPL1 and farnesylated proteins. Mutations in AIPL1 that are linked to LCA abolish its ability to bind farnesylated proteins without compromising the stability of AIPL1. Our study suggests that the critical function of AIPL1 within the photoreceptors requires interactions with farnesylated proteins.

L10 ANSWER 26 OF 33 CAPIUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:650597 CAPIUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 140:26532
TITLE: Delineating the molecular basis of human genetic diseases: epigenetic and functional studies
AUTHOR(S): Akey, Dayna Tirpak
CORPORATE SOURCE: Health Science Center, Univ. of Texas, Houston, TX, USA
SOURCE: (2002) 179 pp. Avail.: UMI, Order No. DA3070963
From: Diss. Abstr. Int., B 2003, 63(11), 5033
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L10 ANSWER 27 OF 33 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2002648220 MEDLINE <<LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 12374762
TITLE: The inherited blindness associated protein AIPL1 interacts with the cell cycle regulator protein NUB1.
AUTHOR: Akey Dayna T; Zhu Xuemei; Dyer Michael; Li Aimin; Sorensen Adam; Blackshaw Seth; Fukuda-Kamitani Taeko; Daiger Stephen P; Craft Cheryl M; Kamitani Tetsu; Sohocki Melanie M
CORPORATE SOURCE: Center for Genome Information, Department of Environmental Health, University of Cincinnati, OH 45267, USA.
CONTRACT NUMBER: EY00395 (NEI)
EY03040 (NEI)
SOURCE: Human molecular genetics, (2002 Oct 15) Vol. 11, No. 22, pp. 2723-33.
Journal code: 9208958. ISSN: 0964-6906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AI844804
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 5 Nov 2002
Last Updated on STN: 18 Mar 2003
Entered Medline: 17 Mar 2003
AB Mutations in the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) gene have been found in patients with Leber congenital amaurosis (LCA), a severe, early-onset form of retinal degeneration. To determine the normal function of AIPL1 and to better understand how mutations in this gene cause disease, we performed a yeast two-hybrid screen to identify AIPL1-interacting proteins in the retina. One of the identified interacting proteins corresponds to NUB1 (NEDD8 Ultimate Buster 1), which is thought to control many biological events, especially cell cycle progression, by downregulating NEDD8 expression. The AIPL1-NUB1 interaction was verified by co-immunoprecipitation studies in Y79 retinoblastoma cells, demonstrating that this interaction occurs within cells that share a number of features with retinal progenitor cells. Furthermore, we examined the localization of the AIPL1 protein within developing and adult retinas, and found that AIPL1 is present in the developing photoreceptor layer of the human retina and within the photoreceptors of the adult retina. Similar to AIPL1

, NUB1 is also expressed in the developing and adult retina. Therefore, it is possible that the early-onset form of retinal degeneration seen in LCA patients with AIPL1 mutations may be due to a defect in the regulation of cell cycle progression during photoreceptor maturation. These data raise the possibility that AIPL1 is important for appropriate photoreceptor formation during development and/or survival following differentiation.

L10 ANSWER 28 OF 33 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2002196859 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 11929855
TITLE: The Leber congenital amaurosis gene product AIPL1
is localized exclusively in rod photoreceptors of the adult
human retina.
AUTHOR: van der Spuy Jacqueline; Chapple J Paul; Clark Brian J;
Luthert Philip J; Sethi Charanjit S; Cheetham Michael E
CORPORATE SOURCE: Department of Pathology, Institute of Ophthalmology,
University College London, Bath Street, London EC1V 9EL,
UK.
SOURCE: Human molecular genetics, (2002 Apr 1) Vol. 11, No. 7, pp.
823-31.
Journal code: 9208958. ISSN: 0964-6906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 4 Apr 2002
Last Updated on STN: 12 Sep 2002
Entered Medline: 11 Sep 2002

AB Leber congenital amaurosis (LCA) is the most severe inherited retinal dystrophy resulting in markedly impaired vision or blindness at birth. LCA is characterized by an extinguished electroretinogram in infancy, which is thought to be indicative of an early and severe impairment of both the rod and cone photoreceptors in the human retina. Recently, the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) gene was identified as the fourth causative gene of LCA. AIPL1 encodes a 384 amino acid protein of unknown function. We have generated a polyclonal antibody against a peptide from a unique region within the primate AIPL1 protein, which detects a protein of approximately 43 kDa in human retinal extracts. A screen of human tissues and immortalized cell lines with this antibody reveals AIPL1 to be specific to human retina and cell lines of retinal origin (Y79 retinoblastoma cells). Within the retina, AIPL1 was detected only in the rod photoreceptor cells of the peripheral and central human retina. The AIPL1 staining pattern extended within the rod photoreceptor cells from the inner segments, through the rod nuclei to the rod photoreceptor synaptic spherules in the outer plexiform layer. AIPL1 was not detected in the cone photoreceptors of peripheral or central human retina. This study is the first to suggest that AIPL1 performs a function essential to the maintenance of rod photoreceptor function.

L10 ANSWER 29 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN
ACCESSION NUMBER: 2003:155437 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200300155437
TITLE: NUB1, a Protein Involved in the Regulation of Apoptosis and
Cell Cycle Progression, Interacts With AIPL1, a
Protein Associated With Leber Congenital Amaurosis.
AUTHOR(S): Shi, G. [Reprint Author]; Akey, D. T.; Zhu, X.;
Fukada-Kamitani, T.; Sorensen, A. F. [Reprint Author];

Daiger, S. P.; Craft, C. M.; Kamitani, T.; Sohocki, M. M.
[Reprint Author]

CORPORATE SOURCE: Ophthalmology, Columbia University, New York, NY, USA
SOURCE: ARVO Annual Meeting Abstract Search and Program Planner,
(2002) Vol. 2002, pp. Abstract No. 3615. cd-rom.

Meeting Info.: Annual Meeting of the Association For
Research in Vision and Ophthalmology. Fort Lauderdale,
Florida, USA. May 05-10, 2002.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Mar 2003
Last Updated on STN: 26 Mar 2003

AB Purpose: We previously identified the aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1) gene, mutations of which cause approximately 10% of Leber congenital amaurosis. As AIPL1 is a novel gene, it is necessary to determine its normal function as the next step toward understanding the molecular and biochemical cause of blindness in these patients. The presence of three highly conserved tetratricopeptide (TPR) motifs in the AIPL1 protein sequence suggested a role as a chaperone protein and made yeast-two hybrid studies a promising approach to determine a potential target of this activity. Methods: The bovine Aipl1 cDNA in the pGBK-T7 vector was the bait in a GAL4 yeast-two hybrid testing system to screen a bovine retinal cDNA library (W. Baehr). Prey plasmids were isolated from the positive clones of the library screening and were co-transformed with either the bait or the empty pGBK-T7 vector into the yeast cells to confirm the interactions. The human ortholog was then tested to confirm that the human proteins could also interact in this system. For further confirmation, co-immunoprecipitation (Co-IP) was performed in COS cells using FLAG-AIPL1 and several controls. Results: Two independent NUB1 (NEDD8 Ultimate Buster-1) clones were identified in the yeast-two hybrid screen, and human AIPL1 also interacted with NUB1 in this system. Co-IP experiments confirmed the positive interaction of NUB1 with AIPL1, as only FLAG-AIPL1, and none of the controls, could co-immunoprecipitate endogenous NUB1 from the COS cells. Conclusion: NUB1 is a negative regulator of the NEDD8 conjugation system, which regulates many biological events, including cell cycle transition and apoptosis. Data from the current study suggest NUB1 as the target of AIPL1 chaperone activity. It is possible that mutated AIPL1 in patients interferes with the ability of AIPL1 to chaperone or translocate NUB1 into the nucleus, resulting in the accumulation of NUB1 in the cytosol. This accumulation may be the cause of cell death and retinal degeneration in these patients. Supported by the Kirchgessner Foundation, the Knights Templar Eye Foundation, the Foundation Fighting Blindness, Fight for Sight, Research Division of Prevent Blindness America, the RPB, and NIH grants EY00395 and EY03040.

L10 ANSWER 30 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2001:342096 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100342096

TITLE: Heterologous expression and purification of the Leber
congenital amaurosis 4 gene product AIPL1.

AUTHOR(S): van der Spuy, J. .[Reprint author]; Cheetham, M. E. [Reprint
author]

CORPORATE SOURCE: Department of Pathology, Institute of Ophthalmology, UCL,
London, UK

SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S655. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale,

Florida, USA. April 29-May 04, 2001. Association for Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jul 2001
Last Updated on STN: 19 Feb 2002

L10 ANSWER 31 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:23346 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200200023346
TITLE: Aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1): A possible function in photoreceptor-specific regulation of apoptosis.
AUTHOR(S): Sonocki, M. M. [Reprint author]; Dalger, S. P. [Reprint author]; Akey, D. T. [Reprint author]; Zhu, X.; Craft, C.
CORPORATE SOURCE: Hum Genet Ctr, Univ TX Health Sci Ctr, Houston, TX, USA
SOURCE: American Journal of Human Genetics, (October, 2001) Vol. 69, No. 4 Supplement, pp. 654. print.
Meeting Info.: 51st Annual Meeting of the American Society of Human Genetics. San Diego, California, USA. October 12-16, 2001.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Dec 2001
Last Updated on STN: 25 Feb 2002

L10 ANSWER 32 OF 33 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:895127 SCISEARCH <>LOGINID::20060824>>
THE GENUINE ARTICLE: 483RD
TITLE: Aryl-hydrocarbon receptor interacting protein-like 1 (AIPL1): a possible function in photoreceptor-specific regulation of apoptosis.
AUTHOR: Sohocki M M (Reprint); Daiger S P; Akey D T; Zhu X; Craft C
CORPORATE SOURCE: Univ Texas, Hlth Sci Ctr, Ctr Human Genet, Houston, TX USA; Univ So Calif, Keck Sch Med, Doheny Eye Inst, Los Angeles, CA 90033 USA
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 2001) Vol. 69, No. 4, Supp. [1], pp. 654-654. MA 2784.
ISSN: 0002-9297.
PUBLISHER: UNIV CHICAGO PRESS, 1427 E 60TH ST, CHICAGO, IL 60637-2954 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 21 Nov 2001

L10 ANSWER 33 OF 33 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001359740 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 11420621
TITLE: Comparative analysis of aryl-hydrocarbon receptor interacting protein-

like 1 (Aip1l), a gene associated with
 inherited retinal disease in humans.
AUTHOR: Sohocki M M; Sullivan L S; Tirpak D L; Daiger S P
CORPORATE SOURCE: Human Genetics Center, School of Public Health, P.O. Box
 20186, Houston, Texas 77225-0334, USA.
CONTRACT NUMBER: EY07142 (NEI)
SOURCE: Mammalian genome : official journal of the International
 Mammalian Genome Society, (2001 Jul) Vol. 12, No. 7, pp.
 566-8.
PUB. COUNTRY: Journal code: 9100916. ISSN: 0938-8990.
DOCUMENT TYPE: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
OTHER SOURCE: Priority Journals
 GENBANK-AF148864; GENBANK-AF180340; GENBANK-AF296410;
 GENBANK-AF296411; GENBANK-AF296412; GENBANK-AF296413;
 GENBANK-AF296414; GENBANK-AF296415
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 3 Sep 2001
 Last Updated on STN: 3 Sep 2001
 Entered Medline: 30 Aug 2001

AB Mutations in AIPL1 cause Leber congenital amaurosis (LCA), the most severe form of inherited blindness in children; however, the function of this protein in normal vision remains unknown. To determine amino acid subsequences likely to be important for function, we have compared the protein sequence of several species. Sequence conservation is highest across the three Aip1l tetratricopeptide (TPR) motifs and extends across the protein, except for a proline-rich amino acid sequence present only at the C-terminus of primate Aip1l. The length of the proline-rich region varies within primates; however, the length differences between human and primate Aip1l do not correlate with evolutionary distance. These observations reinforce the importance of the TPR domains for function, the similarity of Aip1l to a family of proteins that act as molecular chaperones, and the importance of comparative sequencing data for determination of whether AIPL1 sequence variants in patients are likely to cause retinopathy.

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L1 FILE 'REGISTRY' ENTERED AT 18:56:18 ON 24 AUG 2006
2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L2 FILE 'CPLUS' ENTERED AT 18:57:29 ON 24 AUG 2006
2 L1
L3 36 AIPL1

FILE 'MEDLINE, BIOSIS, CPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
18:58:27 ON 24 AUG 2006
L4 268 AIPL1
L5 77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (
L6 69 L4 AND L5
L7 276 L4 OR L5
L8 6 TRP278X AND L7
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:01:11 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:47 ON 24 AUG 2006
L10 33 DUP REM L6 (36 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:59 ON 24 AUG 2006

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FILE 'MEDLINE, BIOSIS, CPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:35:29 ON 24 AUG 2006

=> l7 not l10
L11 243 L7 NOT L10

=> py>2001 and l11
L12 184 PY>2001 AND L11

=> l11 not l12

L13 59 L11 NOT L12

=> dupr rem 113

MISSING OPERATOR REM L13

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> dup rem 113

PROCESSING COMPLETED FOR L13

L14 27 DUP REM L13 (32 DUPLICATES REMOVED)

=> d ibib abs l14 1-27

L14 ANSWER 1 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 1

ACCESSION NUMBER: 2001:342095 BIOSIS <> LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100342095
TITLE: Yeast two-hybrid analysis of AIP11-binding proteins.
AUTHOR(S): Tirpak, D. L. [Reprint author]; Sohocki, M. M. [Reprint author]; Craft, C. M.; Daiger, S. P. [Reprint author]
CORPORATE SOURCE: Human Genetics Center, Univ. of Texas-Houston, Houston, TX, USA
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S655. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001. Association for Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jul 2001
Last Updated on STN: 19 Feb 2002

L14 ANSWER 2 OF 27 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:604566 SCISEARCH <> LOGINID::20060824>>
THE GENUINE ARTICLE: 427EP
TITLE: Heterologous expression and purification of the Leber congenital amaurosis 4 gene product AIP11.
AUTHOR: van der Spuy J (Reprint); Cheetham M E
CORPORATE SOURCE: Univ Coll London, Inst Ophthalmol, Dept Pathol, London, England
COUNTRY OF AUTHOR: England
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (15 MAR 2001 Vol. 42, No. 4, Supp. [S], pp. S655-S655. MA 3523.
ISSN: 0146-0404.
PUBLISHER: ASSOC RESEARCH VISION OPHTHALMOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 10 Aug 2001
Last Updated on STN: 10 Aug 2001

L14 ANSWER 3 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:348209 BIOSIS <> LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100348209
TITLE: Localisation of the genes involved in several autosomal dominant retinal dystrophies.
AUTHOR(S): Van Lith-Verhoeven, J. J. C. [Reprint author]; Hoyng, C. B. [Reprint author]; Deutman, A. F. [Reprint author]; Sohocki,

CORPORATE SOURCE: M. M.; Cremers, F. P. M.
SOURCE: Ophthalmology, St Radboud Hospital, Nymegen, Netherlands
IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S647. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale,
Florida, USA. April 29-May 04, 2001. Association for
Research in Vision and Ophthalmology.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Jul 2001
Last Updated on STN: 19 Feb 2002

L14 ANSWER 4 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:348203 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100348203
TITLE: Family collection and candidate gene analysis of genetic
eye diseases.
AUTHOR(S): Zhang, Q. J. [Reprint author]; Xiao, X. S. [Reprint
author]; Li, S. Q. [Reprint author]; Zhang, F. S.; Guo, X.
M. [Reprint author]; Jia, X. Y. [Reprint author]; Shen, H.
X. [Reprint author]; Li, J. Z.; Li, W. [Reprint author];
Yang, L. P. [Reprint author]
CORPORATE SOURCE: Ocular Genetics and Molecular Biology, Zhongshan Ophthalmic
Center, Sun Yat-Sen University of Medical Sciences,
Guangzhou, 510060, China
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S646. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale,
Florida, USA. April 29-May 04, 2001. Association for
Research in Vision and Ophthalmology.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Jul 2001
Last Updated on STN: 19 Feb 2002

L14 ANSWER 5 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2
ACCESSION NUMBER: 2001:348199 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100348199
TITLE: Genotype-phenotype correlation in LCA patients with
AIPL1 mutations.
AUTHOR(S): Dharmaraj, S. [Reprint author]; Sohocki, M.; Leroy, B. P.;
Birch, D.; Izquierdo, N.; Koenekoop, R. K.; Holder, G. E.;
Bhattacharya, S. S.; Bird, A. C.; Maumenee, I. H. [Reprint
author]
CORPORATE SOURCE: Johns Hopkins Ctr for Hereditary Eye Diseases, Baltimore,
MD, USA
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S645. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale,
Florida, USA. April 29-May 04, 2001. Association for
Research in Vision and Ophthalmology.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Jul 2001
Last Updated on STN: 19 Feb 2002

L14 ANSWER 6 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3

ACCESSION NUMBER: 2001:348197 BIOSIS <<LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100348197
TITLE: Role of AIPL1 in LCA and related inherited
retinal diseases.
AUTHOR(S): Sohocki, M. M. [Reprint author]; Tirpak, D. L. [Reprint
author]; Daiger, S. P. [Reprint author]; Dhamaraj, S.;
Maumenee, I. H.; Birch, D. G.; Heckenlively, J. R.;
Koenekoop, R. K.
CORPORATE SOURCE: Human Genetics Center and Dept of Ophthalmology, Univ of
TX-Houston, Houston, TX, USA
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S645. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology. Fort Lauderdale,
Florida, USA. April 29-May 04, 2001. Association for
Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jul 2001
Last Updated on STN: 19 Feb 2002

L14 ANSWER 7 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:70215 BIOSIS <<LOGINID::20060824>>
DOCUMENT NUMBER: PREV200200070215
TITLE: Towards the identification of at least 12 genes in Leber
congenital amaurosis.
AUTHOR(S): Perrault, I. [Reprint author]; Gerber, S. [Reprint author];
Hanein, S. [Reprint author]; Rozet, J.-M. [Reprint author];
Ducrocq, D. [Reprint author]; Barbet, F. [Reprint author];
Ghazi, I.; Dufier, J.-L.; Munnich, A. [Reprint author];
Kaplan, J. [Reprint author]
CORPORATE SOURCE: Laboratoire de Recherches sur les Handicaps Genetiques de
l'Enfant, INSERM U393, Hopital des Enfants Malades, PARIS
Cedex, 15, France
SOURCE: American Journal of Human Genetics, (October, 2001) Vol.
69, No. 4 Supplement, pp. 628. print.
Meeting Info.: 51st Annual Meeting of the American Society
of Human Genetics. San Diego, California, USA. October
12-16, 2001.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2002
Last Updated on STN: 25 Feb 2002

L14 ANSWER 8 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:70121 BIOSIS <<LOGINID::20060824>>
DOCUMENT NUMBER: PREV200200070121
TITLE: Identification of a novel GUCY2D mutation in an Iranian
family with Leber Congenital Amaurosis.
AUTHOR(S): Rezaie, T. [Reprint author]; Karimi-Nejad, M. H.; Meshkat,
M.; Sohbati, S.; Karimi-Nejad, R.; Najmabadi, H.;
Sarfarazi, M. [Reprint author]
CORPORATE SOURCE: Molecular Ophthalmic Genetics, Univ of Connecticut Health
Center, Farmington, CT, USA
SOURCE: American Journal of Human Genetics, (October, 2001) Vol.
69, No. 4 Supplement, pp. 612. print.
Meeting Info.: 51st Annual Meeting of the American Society
of Human Genetics. San Diego, California, USA. October
12-16, 2001.

CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2002
Last Updated on STN: 25 Feb 2002

L14 ANSWER 9 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 2001:356432 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200100356432
TITLE: Comparative analysis of aryl-hydrocarbon receptor interacting protein-like 1 (Aipl1), a gene associated with inherited retinal disease in humans.
AUTHOR(S): Sohocki, Melanie M. [Reprint author]; Sullivan, Lori S.; Tirpak, Dayna L.; Daiger, Stephen P.
CORPORATE SOURCE: Human Genetics Center, School of Public Health, Houston, TX, 77225-0334, USA
msohocki@sph.uth.tmc.edu
SOURCE: Mammalian Genome, (July, 2001) Vol. 12, No. 7, pp. 566-568.
print.
CODEN: MAMGEC. ISSN: 0938-8990.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2001
Last Updated on STN: 19 Feb 2002

AB Mutations in AIPL1 cause Leber congenital amaurosis (LCA), the most severe form of inherited blindness in children; however, the function of this protein in normal vision remains unknown. To determine amino acid subsequences likely to be important for function, we have compared the protein sequence of several species. Sequence conservation is highest across the three Aipl1 tetratricopeptide (TPR) motifs and extends across the protein, except for a proline-rich amino acid sequence present only at the C-terminus of primate Aipl1. The length of the proline-rich region varies within primates; however, the length differences between human and primate Aipl1 do not correlate with evolutionary distance. These observations reinforce the importance of the TPR domains for function, the similarity of Aipl1 to a family of proteins that act as molecular chaperones, and the importance of comparative sequencing data for determination of whether AIPL1 sequence variants in patients are likely to cause retinopathy.

L14 ANSWER 10 OF 27 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001297312 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 11377968
TITLE: Molecular genetics and prospects for therapy of the inherited retinal dystrophies.
AUTHOR: Bessant D A; Ali R R; Bhattacharya S S
CORPORATE SOURCE: Department of Molecular Genetics, Institute of Ophthalmology, University College London, Bath Street, EC1V 9EL, London, UK.
SOURCE: Current opinion in genetics & development, (2001 Jun) Vol. 11, No. 3, pp. 307-16. Ref: 69
Journal code: 9111375. ISSN: 0959-437X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111

ENTRY DATE: Entered STN: 5 Nov 2001
Last Updated on STN: 5 Nov 2001
Entered Medline: 1 Nov 2001

AB More than 60 genes responsible for human retinal dystrophies have been identified. Those recently isolated include the transcription factor genes NRL and NR2E3, RDH5 (retinol dehydrogenase), EFEMP1 (which encodes an extracellular matrix protein), CRB1, PROML1, RP1, AIPL1 and USH1C (harmonin). The ABCR protein has been identified as a critical transporter in the recycling of retinal (vitamin A). At present, a number of novel therapeutic strategies are being evaluated including pharmacological treatments, cell transplantation and gene therapy. The progress made with such approaches now offers hope to patients with these incurable forms of blindness.

L14 ANSWER 11 OF 27 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001497731 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 11548141
TITLE: Leber's congenital amaurosis with anterior keratoconus in Pakistani families is caused by the Trp278X mutation in the AIPL1 gene on 17p.
AUTHOR: Damji K F; Sohocki M M; Khan R; Gupta S K; Rahim M; Loyer M; Hussein N; Karim N; Ladak S S; Jamal A; Bulman D; Koenekoop R K
CORPORATE SOURCE: Ottawa Hospital Research Institute, Ont..
kdamji@ottahospital.on.ca
SOURCE: Canadian journal of ophthalmology. Journal canadien d'ophtalmologie, (2001 Aug) Vol. 36, No. 5, pp. 252-9.
Journal code: 0045312. ISSN: 0008-4182.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 10 Sep 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 14 Jan 2002

AB BACKGROUND: Leber's congenital amaurosis (LCA) represents the earliest and severest form of retinal dystrophy leading to congenital blindness. A total of 20% of children attending blind schools have this disease. LCA has a multigenic basis and is proving central to our understanding of the development of the retina. We describe the clinical and molecular genetic features of four inbred pedigrees from neighbouring remote villages in northern Pakistan, in which some of the affected members have concurrent keratoconus. METHODS: History-taking and physical and eye examinations were performed in the field. Venipuncture, DNA extraction, studies of linkage to known LCA genes, automated sequencing and polymorphism analyses for haplotype assessments were done. RESULTS: We examined 12 affected and 15 unaffected family members. By history, there were an additional nine blind people in the four pedigrees. In each pedigree a consanguineous marriage was evident. We found a homozygous nonsense mutation in the AIPL1 gene, which replaces a tryptophan with a stop codon (Trp278X). The phenotype is severe and variable, despite the common molecular genetic etiology in each family. Affected patients had hand motion to no light perception vision and fundus findings ranging from maculopathy to diffuse pigmentary retinopathy. Three affected members had definite keratoconus, and two were suspects based on mild cone formation in the cornea of at least one eye. INTERPRETATION: We have identified four Pakistani families with a severe form of LCA that is associated with severe keratoconus in some affected members. The molecular etiology in all four families is a homozygous nonsense mutation, Trp278X, in the photoreceptor-pineal gene AIPL1. To our knowledge, this is one of the first phenotype-genotype correlations of AIPL1-associated

LCA.

L14 ANSWER 12 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:282171 BIOSIS <>LOGINID::20060824>>

DOCUMENT NUMBER: PREV200100282171

TITLE: The Southwest Eye Registry: A regional database for patients with inherited retinal disorders.

AUTHOR(S): Wheaton, D. H. [Reprint author]; Sullivan, L. S.; Daiger, S. P.; Birch, D. G. [Reprint author]

CORPORATE SOURCE: Retina Foundation of the SW, Dallas, TX, USA

SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S75. print.

Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Jun 2001

Last Updated on STN: 19 Feb 2002

L14 ANSWER 13 OF 27 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2001124908 MEDLINE <>LOGINID::20060824>>

DOCUMENT NUMBER: PubMed ID: 11139241

TITLE: Prevalence of mutations causing retinitis pigmentosa and other inherited retinopathies.

AUTHOR: Sohocki M M; Daiger S P; Bowne S J; Rodriguez J A; Northrup H; Heckenlively J R; Birch D G; Mintz-Hittner H; Ruiz R S; Lewis R A; Saperstein D A; Sullivan L S

CORPORATE SOURCE: Human Genetics Center, School of Public Health, University of Texas-Houston Health Science Center, Houston, Texas, USA.

CONTRACT NUMBER: EY05235 (NEI)
EY07142 (NEI)

SOURCE: Human mutation, (2001) Vol. 17, No. 1, pp. 42-51.
Journal code: 9215429. E-ISSN: 1098-1004.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 21 May 2001
Entered Medline: 22 Feb 2001

AB Inherited retinopathies are a genetically and phenotypically heterogeneous group of diseases affecting approximately one in 2000 individuals worldwide. For the past 10 years, the Laboratory for Molecular Diagnosis of Inherited Eye Diseases (LMDIED) at the University of Texas-Houston Health Science Center has screened subjects ascertained in the United States and Canada for mutations in genes causing dominant and recessive autosomal retinopathies. A combination of single strand conformational analysis (SSCA) and direct sequencing of five genes (rhodopsin, peripherin/RDS, RP1, CRX, and AIPL1) identified the disease-causing mutation in approximately one-third of subjects with autosomal dominant retinitis pigmentosa (adRP) or with autosomal dominant cone-rod dystrophy (adCORD). In addition, the causative mutation was identified in 15% of subjects with Leber congenital amaurosis (LCA). Overall, we report identification of the causative mutation in 105 of 506 (21%) of unrelated subjects (probands) tested; we report five previously unreported mutations in rhodopsin, two in peripherin/RDS, and one previously unreported mutation in the cone-rod homeobox gene, CRX. Based on this large survey, the prevalence of disease-causing mutations in each

of these genes within specific disease categories is estimated. These data are useful in estimating the frequency of specific mutations and in selecting individuals and families for mutation-specific studies.
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L14 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:438122 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 137:383251
TITLE: Functional analysis of AIPL1: A novel photoreceptor-pineal specific protein causing Leber congenital amaurosis and other retinopathies
AUTHOR(S): Sohocki, Melanie M.; Tirpak, Dayna L.; Craft, Cheryl M.; Daiger, Stephen P.
CORPORATE SOURCE: Human Genetics Center and Dept. of Ophthalmology and Visual Science, The Univ. of Texas, Houston, USA
SOURCE: New Insights into Retinal Degenerative Diseases, [Proceedings of the International Symposium on Retinal Degeneration], 9th, Durango, CO, United States, Oct. 9-14, 2000 (2001), Meeting Date 2000, 37-44. Editor(s): Anderson, Robert E.; LaVail, Matthew M.; Hollyfield, Joe G. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69CSG5; ISBN: 0-306-46679-1
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A comparative sequencing of AIPL1 orthologs between mammalian species and yeast two-hybrid analyses were conducted to detect AIPL1-binding proteins. Results reveal a high degree of sequence conservation across AIPL1 proteins, at least within mammals, and reinforce the structural relation of AIPL1 to the Fkbp families of proteins, which function as mol. chaperones in steroid receptor signaling, heat shock responses, and immunosuppression. The increased sequence conservation within the tetratricopeptide motifs suggests an important role for these motifs in protein function. Moreover, the conservation of certain residues within the proline-rich region suggests that they may be important for primate AIPL1 function. Yeast two-hybrid analyses identified two potential AIPL1-interacting proteins, clone #7 which is homologous to a glucose metabolism gene on human 5q and clone #16, homologous to a gene on human 15p.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 27 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001074394 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 10961990
TITLE: Binding of aryl hydrocarbon receptor (AhR) to AhR-interacting protein. The role of hsp90.
AUTHOR: Bell D R; Poland A
CORPORATE SOURCE: Centers for Disease Control, National Institute for Occupational Safety and Health, Health Effects Laboratory Division, Morgantown, West Virginia 26505, USA..
david.bell@nottingham.ac.uk
SOURCE: The Journal of biological chemistry, (2000 Nov 17) Vol. 275, No. 46, pp. 36407-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001

Entered Medline: 29 Dec 2000

AB The aryl hydrocarbon receptor (AhR) has been shown to interact with an immunophilin-like molecule known as AhR-interacting protein (AIP) and to enhance AhR function. We show here that AIP associates with AhR homologues from mouse and fish, which can bind ligands such as dioxin, but nonligand binding homologues from *Caenorhabditis elegans* or *Drosophila* do not bind to AIP. However, a minimal ligand-binding domain of the AhR is incapable of binding AIP. The binding of AIP to AhR in reticulocyte lysate shows several of the characteristics of an hsp90-dependent process, including sensitivity to geldanamycin and temperature and a requirement for ATP or nonhydrolyzable analogues. Purified AIP binds to the C terminus of hsp90, and mutation of a conserved basic residue in the tetratricopeptide repeats of AIP (K266A, analogous to K97A in protein phosphatase 5) abolishes binding to hsp90. Mutation of K266A in AIP reduces binding to AhR by 75-80%; the geldanamycin sensitivity of this complex shows that AhR stabilizes the AIP-hsp90-AhR complex. The alpha-helical C terminus of AIP, which is outside the tetratricopeptide repeat domain, is absolutely required for binding to AhR as shown by deletions of the C-terminal 5 amino acids or alanine-scanning mutagenesis, but it is not required for binding of AIP to hsp90. The data support a model where 1) AIP binds to both hsp90 and AhR; 2) hsp90 is required for AhR-AIP binding; and 3) the binding of AhR to AIP stabilizes the AIP-hsp90-AhR complex.

L14 ANSWER 16 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 9
ACCESSION NUMBER: 2000:488864 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000488985
TITLE: Molecular studies of AIPL1, a gene causing Leber congenital amaurosis.
AUTHOR(S): Tirpak, D. L. [Reprint author]; Sohocki, M. M. [Reprint author]; Craft, C. M.; Daiger, S. P. [Reprint author]
CORPORATE SOURCE: Human Genetics Center, University of Texas-Houston, Houston, TX, USA
SOURCE: American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 411. print.
Meeting Info.: 50th Annual Meeting of the American Society of Human Genetics. Philadelphia, Pennsylvania, USA. October 03-07, 2000. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002

L14 ANSWER 17 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 10
ACCESSION NUMBER: 2000:491193 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000491314
TITLE: Comparative sequencing of aryl-hydrocarbon interacting protein like-1 (AIPL1), a protein associated with Leber congenital amaurosis.
AUTHOR(S): Sohocki, M. M. [Reprint author]; Tirpak, D. T. [Reprint author]; Daiger, S. P. [Reprint author]
CORPORATE SOURCE: Human Genetics Ctr, Univ Texas-Houston Health Sci Ctr, Houston, TX, USA
SOURCE: American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 388. print.
Meeting Info.: 50th Annual Meeting of the American Society of Human Genetics. Philadelphia, Pennsylvania, USA. October

03-07, 2000. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002

L14 ANSWER 18 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN DUPLICATE 11

ACCESSION NUMBER: 2000:488756 BIOSIS <> LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000488877

TITLE: Leber Congenital Amaurosis with anterior keratoconus in Pakistani families is caused by the Trp278X mutation in the AIPL1 gene on 17p.

AUTHOR(S): Damji, K. F. [Reprint author]; Sohocki, M. M.; Khan, R.; Gupta, S. K. [Reprint author]; Rahim, M.; Loyer, M.; Hussein, N.; Karim, N.; Ladak, S. S.; Jamal, A.; Bulman, D. [Reprint author]; Koenekoop, R. K.

CORPORATE SOURCE: Ottawa Hospital Research Institute, Ottawa, ON, Canada
SOURCE: American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 382. print.
Meeting Info.: 50th Annual Meeting of the American Society of Human Genetics. Philadelphia, Pennsylvania, USA. October 03-07, 2000. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002

L14 ANSWER 19 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2000:241492 BIOSIS <> LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000241492

TITLE: Analysis of the AIPL1 gene in Belgian and British patients with Leber congenital amaurosis.

AUTHOR(S): Aragon-Martin, J. A. [Reprint author]; Leroy, B. P. [Reprint author]; Prescott, Q. C. [Reprint author]; Sohocki, M. M.; Daiger, S. P.; Bird, A. C.; Meire, F. M.; Payne, A. M. [Reprint author]; Bhattacharya, S. S. [Reprint author]

CORPORATE SOURCE: Dept. of Molecular Genetics, Inst. of Ophthalmology, London, UK
SOURCE: IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S196. print.
Meeting Info.: Annual Meeting of the Association in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L14 ANSWER 20 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2000:250470 BIOSIS <> LOGINID::20060824>>

DOCUMENT NUMBER: PREV200000250470
TITLE: Genetic analysis of six Puerto Rican families with Leber congenital amaurosis.
AUTHOR(S): De Pol, M. E. [Reprint author]; Dharmaraj, S. [Reprint author]; Izquierdo, N.; Li, Y. Y. [Reprint author]; Maumenee, I. H. [Reprint author]
CORPORATE SOURCE: Johns Hopkins Center for Hereditary Eye Diseases, Wilmer Eye Institute Johns Hopkins Hospital, Baltimore, MD, USA
SOURCE: IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S196. print.
Meeting Info.: Annual Meeting of the Association in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L14 ANSWER 21 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:241489 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000241489
TITLE: Physical mapping of the gene for CORD5 on human chromosome 17p.
AUTHOR(S): Small, K. W. [Reprint author]; Yelchits, S. [Reprint author]; Forsman, K.; Sheikhabandi, S. [Reprint author]; Shirvani, A. [Reprint author]; Nguyen, R. N. [Reprint author]; Vyas, P. R. [Reprint author]; Sohocki, M. M.; Daiger, S. P.; Udar, N. S. [Reprint author]
CORPORATE SOURCE: Ophthalmology, UCLA/Jules Stein Eye Institute, Los Angeles, CA, USA
SOURCE: IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S195. print.
Meeting Info.: Annual Meeting of the Association in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L14 ANSWER 22 OF 27 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2000402727 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 10873396
TITLE: Prevalence of AIPL1 mutations in inherited retinal degenerative disease.
AUTHOR: Sohocki M M; Perrault I; Leroy B P; Payne A M; Dharmaraj S; Bhattacharya S S; Kaplan J; Maumenee I H; Koeneekoop R; Meire F M; Birch D G; Heckenlively J R; Daiger S P
CORPORATE SOURCE: Human Genetics Center, School of Public Health, Houston, Texas, 77225-0334, USA.
CONTRACT NUMBER: EY05235 (NEI)
EY07142 (NEI)
SOURCE: Molecular genetics and metabolism, (2000 Jun) Vol. 70, No. 2, pp. 142-50.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 1 Sep 2000
Last Updated on STN: 1 Sep 2000
Entered Medline: 22 Aug 2000

AB Leber congenital amaurosis (LCA) is the most severe form of inherited retinal dystrophy and the most frequent cause of inherited blindness in children. LCA is usually inherited in an autosomal recessive fashion, although rare dominant cases have been reported. One form of LCA, LCA4, maps to chromosome 17p13 and is genetically distinct from other forms of LCA. We recently identified the gene associated with LCA4, AIPL1 (aryl-hydrocarbon interacting protein-like 1) and identified three mutations that were the cause of blindness in five families with LCA. In this study, AIPL1 was screened for mutations in 512 unrelated probands with a range of retinal degenerative diseases to determine if AIPL1 mutations cause other forms of inherited retinal degeneration and to determine the relative contribution of AIPL1 mutations to inherited retinal disorders in populations worldwide. We identified 11 LCA families whose retinal disorder is caused by homozygous or compound heterozygous AIPL1 mutations. We also identified affected individuals in two apparently dominant families, diagnosed with juvenile retinitis pigmentosa or dominant cone-rod dystrophy, respectively, who are heterozygous for a 12-bp AIPL1 deletion. Our results suggest that AIPL1 mutations cause approximately 7% of LCA worldwide and may cause dominant retinopathy.

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ACCESSION NUMBER: 2000:227755 BIOSIS <>LOGINID::20060824>>
DOCUMENT NUMBER: PREV200000227755
TITLE: Mutations in AIPL1, a novel photoreceptor/pineal-expressed gene on 17p13, cause Leber congenital amaurosis (LCA4).
AUTHOR(S): Sohocki, M. M. [Reprint author]; Perrault, I.; Payne, A. M.; Kaplan, J.; Bhattacharya, S. S.; Birch, D. G.; Heckenlively, J. R.; Daiger, S. P. [Reprint author]
CORPORATE SOURCE: Human Genetics Center, UT-Houston, Houston, TX, USA
SOURCE: IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S94. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

L14 ANSWER 24 OF 27 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:491552 SCISEARCH <>LOGINID::20060824>>
THE GENUINE ARTICLE: 300HF
TITLE: Mutations in AIPL1, a novel photoreceptor/pineal-expressed gene on 17P13, cause leber congenital amaurosis (LCA34).
AUTHOR: Sohocki M M (Reprint); Perrault I; Payne A M; Kaplan J; Bhattacharya S S; Birch D G; Heckenlively J R; Daiger S P
CORPORATE SOURCE: Univ Texas, Ctr Human Genet, Houston, TX USA; Hosp Enfants Malad, INSERM U393, Unite Rech Handicaps Genet Enfant, Paris, France; Univ Coll London, Dept Mol Genet, Inst

COUNTRY OF AUTHOR: Ophthalmol, London, England; Retina Fdn SW, Dallas, TX USA; Univ Calif Los Angeles, Jules Stein Eye Inst, Los Angeles, CA 90024 USA
SOURCE: USA; France; England
) INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (15 MAR 2000
REFERENCE COUNT: Vol. 41, No. 4, Supp. [S], pp. S94-S94. MA 495.
PUBLISHER: ISSN: 0146-0404.
ASSOC RESEARCH VISION OPHTHALMOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
ENTRY DATE: 0
REFERENCE COUNT: Entered STN: 2000
Last Updated on STN: 2000

L14 ANSWER 25 OF 27 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2000082814 MEDLINE <>LOGINID::20060824>>
DOCUMENT NUMBER: PubMed ID: 10615133
TITLE: Mutations in a new photoreceptor-pineal gene on 17p cause Leber congenital amaurosis.
AUTHOR: Sohocki M M; Bowne S J; Sullivan L S; Blackshaw S; Cepko C L; Payne A M; Bhattacharya S S; Khalil S; Qasim Mehdi S; Birch D G; Harrison W R; Elder F F; Heckenlively J R; Daiger S P
CORPORATE SOURCE: Human Genetics Center, School of Public Health, The University of Texas-Houston Health Science Center, Houston, Texas, USA.

CONTRACT NUMBER: EY07142 (NEI)
SOURCE: Nature genetics, (2000 Jan) Vol. 24, No. 1, pp. 79-83.
Journal code: 9216904. ISSN: 1061-4036.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF148864; GENBANK-AF151392; GENBANK-AF180340;
GENBANK-AF180341; GENBANK-AF180472

ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 18 Feb 2000
Last Updated on STN: 18 Feb 2000
Entered Medline: 10 Feb 2000

AB Leber congenital amaurosis (LCA, MIM 204000) accounts for at least 5% of all inherited retinal disease and is the most severe inherited retinopathy with the earliest age of onset. Individuals affected with LCA are diagnosed at birth or in the first few months of life with severely impaired vision or blindness, nystagmus and an abnormal or flat electroretinogram (ERG). Mutations in GUCY2D (reference 3), RPE65 (reference 4) and

CRX (reference 5) are known to cause LCA, but one study identified disease-causing GUCY2D mutations in only 8 of 15 families whose LCA locus maps to 17p13.1 (reference 3), suggesting another LCA locus might be located on 17p13.1. Confirming this prediction, the LCA in one Pakistani family mapped to 17p13.1, between D17S849 and D17S960-a region that excludes GUCY2D. The LCA in this family has been designated LCA4 (reference 6). We describe here a new photoreceptor/pineal-expressed gene, AIPL1 (encoding aryl-hydrocarbon interacting protein-like 1), that maps within the LCA4 candidate region and whose protein contains three tetratricopeptide (TPR) motifs, consistent with nuclear transport or chaperone activity. A homozygous nonsense mutation at codon 278 is present in all affected members of the original LCA4 family. AIPL1 mutations may cause approximately 20% of recessive LCA, as disease-causing mutations were identified in 3 of 14 LCA families not tested previously for linkage.

L14 ANSWER 26 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
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ACCESSION NUMBER: 2000:368720 BIOSIS <>LOGINID::20060824>>
 DOCUMENT NUMBER: PREV200000368720
 TITLE: Extensive screening of four disease causing genes and several candidate genes in 130 families affected with Leber congenital amaurosis.
 AUTHOR(S): Perrault, Isabelle [Reprint author]; Rozet, J.-M. [Reprint author]; Gerber, S. [Reprint author]; Ducrocq, D. [Reprint author]; Ghazi, I.; Leowski, C.; Souied, E. H. [Reprint author]; Dufier, J.-L.; Munnich, A. [Reprint author]; Kaplan, J. [Reprint author]; Rozet, J.-M. [Reprint author]
 CORPORATE SOURCE: Inserm U393, Paris Cedex 15, France
 SOURCE: European Journal of Human Genetics, (June, 2000) Vol. 8, No. Supplement 1, pp. 41. print.
 Meeting Info.: European Human Genetics Conference 2000. Amsterdam, Netherlands. May 27-February 30, 2000. European Society of Human Genetics.
 ISSN: 1018-4813.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 30 Aug 2000
 Last Updated on STN: 8 Jan 2002

L14 ANSWER 27 OF 27 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
 STN DUPLICATE 14

ACCESSION NUMBER: 1999:497396 BIOSIS <>LOGINID::20060824>>
 DOCUMENT NUMBER: PREV199900497396
 TITLE: Human aryl-hydrocarbon interacting protein-like 1 gene (AIPL1), a candidate for inherited retinal disorders: Mapping to 17p13, characterization and mutation testing.
 AUTHOR(S): Sohocki, M. M. [Reprint author]; Blackshaw, S.; Cepko, C. L.; Sullivan, L. S. [Reprint author]; Daiger, S. P. [Reprint author]
 CORPORATE SOURCE: Human Genetics Center, School of Public Health, University of Texas HSC, Houston, TX, USA
 SOURCE: American Journal of Human Genetics, (Oct., 1999) Vol. 65, No. 4, pp. A112. print.
 Meeting Info.: 49th Annual Meeting of the American Society of Human Genetics. San Francisco, California, USA. October 19-23, 1999. The American Society of Human Genetics.
 CODEN: AJHGAG. ISSN: 0002-9297.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 23 Nov 1999
 Last Updated on STN: 23 Nov 1999

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(FILE 'HOME' ENTERED AT 18:55:37 ON 24 AUG 2006)

FILE 'REGISTRY' ENTERED AT 18:56:18 ON 24 AUG 2006
L1 2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

FILE 'CAPLUS' ENTERED AT 18:57:29 ON 24 AUG 2006
L2 2 L1
L3 36 AIPL1

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
18:58:27 ON 24 AUG 2006
L4 268 AIPL1
L5 77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (
L6 69 L4 AND L5
L7 276 L4 OR L5
L8 6 TRP278X AND L7
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:01:11 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:47 ON 24 AUG 2006
L10 33 DUP REM L6 (36 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:59 ON 24 AUG 2006

FILE 'STNGUIDE' ENTERED AT 19:21:06 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:35:29 ON 24 AUG 2006
L11 243 L7 NOT L10
L12 184 PY>2001 AND L11
L13 59 L11 NOT L12
L14 27 DUP REM L13 (32 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:40:29 ON 24 AUG 2006

=> l3 not l14
L14 CANNOT BE SEARCHED IN STNGUIDE
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Enter DISPLAY HISTORY to see the sequence of commands that created
this L-number.

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FULL ESTIMATED COST 0.48 232.82

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FILE 'MEDLINE' ENTERED AT 19:45:05 ON 24 AUG 2006

FILE 'BIOSIS' ENTERED AT 19:45:05 ON 24 AUG 2006
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=> 13 not 114
L15 242 L3 NOT L14

=>

=> 13 not 14
L16 0 L3 NOT L4

=> 13 not 114
L17 242 L3 NOT L14

=> d scan 13

L3 36 ANSWERS CAPLUS COPYRIGHT 2006 ACS on STN
CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
TI Delineating the molecular basis of human genetic diseases: epigenetic and functional studies
ST genetic disease epigenetics human; ankylosing spondylitis DNA methylation human; blindness AIPL1 interacting protein human
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AIPL1 (aryl hydrocarbon receptor-interacting protein-like 1); epigenetic and functional studies of the DNA methylation in human ankylosing spondylitis and AIPL1-associated protein interactions in blindness)
IT Inflammation
Spinal column, disease
(ankylosing spondylitis; epigenetic and functional studies of the DNA methylation in human ankylosing spondylitis and AIPL1-associated protein interactions in blindness)
IT Blindness
Human
Methylation
(epigenetic and functional studies of the DNA methylation in human ankylosing spondylitis and AIPL1-associated protein interactions in blindness)
IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(epigenetic and functional studies of the DNA methylation in human ankylosing spondylitis and AIPL1-associated protein interactions in blindness)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d scan 117

L17 242 ANSWERS BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Abolished interaction of NUB1 with mutant AIPL1 involved in
Leber congenital amaurosis.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L17 242 ANSWERS SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2005:1061539 SCISEARCH
GA The Genuine Article (R) Number: 974IE
TI Interaction of NUB1 with the proteasome subunit S5a
CC BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS
ST Author Keywords: NUBL; NUBL1; AIPL1; NEDD8; ubiquitin;
proteasome; S5a; UBL; UBA
STP KeyWords Plus (R): UBIQUITIN-LIKE PROTEINS; NEDD8 CONJUGATION; EXPRESSION;
DOMAIN
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L17 242 ANSWERS BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI A screen for mutations of the Aipl1 gene in patients with
supernormal scotopic Erg.
IT Miscellaneous Descriptors
visual acuity; scotopic Erg b-wave

L17 242 ANSWERS CAPLUS COPYRIGHT 2006 ACS on STN
CC 14-10 (Mammalian Pathological Biochemistry)
TI AIPL1, a protein implicated in Leber's congenital amaurosis,
interacts with and aids in processing of farnesylated proteins
ST AIPL1 protein eye disease Leber congenital amaurosis
farnesylated protein
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AIPL1 (aryl hydrocarbon receptor-interacting protein-like
1); AIPL1, a protein implicated in Leber's congenital
amaurosis, interacts with and aids in processing of farnesylated
proteins)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(AIPL1; To understand the mol. basis of LCA caused by aryl
hydrocarbon receptor-interacting protein-like 1 (AIPL1)
mutations authors performed a yeast two-hybrid screen using
AIPL1 as bait)

IT Isoprenylation
(Anal. of isoprenylation in cultured human cells shows that
AIPL1 enhances the processing of farnesylated proteins)

IT Eye, disease
(Leber congenital amaurosis; AIPL1, a protein implicated in
Leber's congenital amaurosis, interacts with and aids in processing of
farnesylated proteins)

IT Human
(cultured human cells; Anal. of isoprenylation in cultured human cells
shows that AIPL1 enhances the processing of farnesylated
proteins)

IT Photoreceptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(essential function of AIPL1 within photoreceptors requires

interactions with farnesylated proteins)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(farnesylated; AIPL1, a protein implicated in Leber's
congenital amaurosis, interacts with and aids in processing of
farnesylated proteins)
IT Mutation
(of AIPL1 gene; To understand the mol. basis of LCA caused by
aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1)
mutations authors performed a yeast two-hybrid screen using
AIPL1 as bait)
L17 242 ANSWERS SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2000:912185 SCISEARCH
GA The Genuine Article (R) Number: 355TA
TI Leber Congenital Amaurosis with anterior keratoconus in Pakistani families
is caused by the Trp278X mutation in the AIPL1 gene on 17p.
CC GENETICS & HEREDITY

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> Trp? and l17
L18 6 TRP? AND L17

=> d his

(FILE 'HOME' ENTERED AT 18:55:37 ON 24 AUG 2006)

FILE 'REGISTRY' ENTERED AT 18:56:18 ON 24 AUG 2006

L1 2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

FILE 'CAPLUS' ENTERED AT 18:57:29 ON 24 AUG 2006

L2 2 L1
L3 36 AIPL1

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
18:58:27 ON 24 AUG 2006

L4 268 AIPL1
L5 77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L6 69 L4 AND L5
L7 276 L4 OR L5
L8 6 TRP278X AND L7
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:01:11 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:47 ON 24 AUG 2006

L10 33 DUP REM L6 (36 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:15:59 ON 24 AUG 2006

FILE 'STNGUIDE' ENTERED AT 19:21:06 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:35:29 ON 24 AUG 2006

L11 243 L7 NOT L10
L12 184 PY>2001 AND L11
L13 59 L11 NOT L12
L14 27 DUP REM L13 (32 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:40:29 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
19:45:05 ON 24 AUG 2006

L15 242 L3 NOT L14
L16 0 L3 NOT L4
L17 242 L3 NOT L14
L18 6 TRP? AND L17

=> l18 not 18
L19 2 L18 NOT L8

=> dup rem 119
PROCESSING COMPLETED FOR L19
L20 2 DUP REM L19 (0 DUPLICATES REMOVED)

=> d ibib abs l20 1-2

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:769226 CAPLUS <<LOGINID::20060824>>
TITLE: Detection of somatic mutation in blood in the early
diagnosis of cancer
INVENTOR(S): North, Don Adams
PATENT ASSIGNEE(S): Sky Genetics, Inc., USA
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|------------|
| WO 2006081248 | A2 | 20060803 | WO 2006-US2500 | 20060124 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | |
| US 2006183893 | A1 | 20060817 | US 2005-311594 | 20051219 |
| PRIORITY APPLN. INFO.: | | | US 2005-646961P | P 20050125 |
| | | | US 2005-669639P | P 20050408 |
| | | | US 2005-311594 | A 20051219 |

AB A method of cancer diagnosis that involves detection of cancer-associated somatic mutations in peripheral blood is described. Cancer markers are most commonly mutated or abnormal DNA sequences associated with metastatic cancer. Markers may be detected using PCR, microarrays, or other nucleic acid or peptide-based assays. These methods may be used for a variety of diagnostic purposes, including initial, early-stage or later diagnosis of cancer, particularly metastatic cancer and monitoring of cancer or treatment progression. The cancer markers may also be used to create a cancer marker profile. Treatment may be directed based on this profile. Addnl., methods using blood may provide a cancer marker profile of mutations or abnormalities found in at least one of several tumors in the body, instead of merely one tumor. The invention also include kits, such

as primer kits, and microarrays for use in performing the various methods.

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:671727 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:166667
TITLE: The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs
INVENTOR(S): Ueno, Yuki; Tsuda, Takanori; Takanori, Hitoshi; Yoshikawa, Toshikazu; Osawa, Toshihiko
PATENT ASSIGNEE(S): Biomarker Science Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 85 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2005198640 | A2 | 20050728 | JP 2004-53258 | 20040227 |
| PRIORITY APPLN. INFO.: | | | JP 2003-394758 | A 20031125 |

AB The curcuminoids- and anthocyanins-responsive gene expression profiles in adipocytes have been revealed. The curcuminoids- and anthocyanins-responsive genes are designed to be used as the index markers in the screenings of the substances that can affect the gene expression patterns in obesity and diabetes. These substances can be the candidates of anti-obesity and anti-diabetes drugs. Therefore, the groups of curcuminoids- and anthocyanins-responsive genes are intended to be used as markers in a form of kit such as DNA chip for the screening of anti-obesity and anti-diabetes drugs.

=> t ti l3 1-50

L3 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Detection of somatic mutation in blood in the early diagnosis of cancer

L3 ANSWER 2 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Exclusion of LCA5 locus in a consanguineous Turkish family with macular coloboma-type LCA

L3 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Predominant rod photoreceptor degeneration in Leber congenital amaurosis

L3 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs

L3 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Dioxin: a review of its environmental effects and its aryl hydrocarbon receptor biology

L3 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI A missense mutation in GUCY2D acts as a genetic modifier in RPE65-related Leber congenital amaurosis

L3 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Leber congenital amaurosis: A genetic paradigm

L3 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI AIPL1, the protein that is defective in Leber congenital

amaurosis, is essential for the biosynthesis of retinal rod cGMP phosphodiesterase. [Erratum to document cited in CA141:330028]

- L3 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Retinal degeneration in Aip1l-deficient mice: a new genetic model of Leber congenital amaurosis
- L3 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The Leber Congenital Amaurosis Protein AIPL1 Modulates the Nuclear Translocation of NUB1 and Suppresses Inclusion Formation by NUB1 Fragments
- L3 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Purification, characterization and intracellular localization of aryl hydrocarbon interacting protein-like 1 (AIPL1) and effects of mutations associated with inherited retinal dystrophies
- L3 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Use of adeno-associated virus serotype 4 in mediating transduction of retinal pigmented epithelium of mammals after subretinal delivery
- L3 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI AIPL1, the protein that is defective in Leber congenital amaurosis, is essential for the biosynthesis of retinal rod cGMP phosphodiesterase
- L3 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Leber congenital amaurosis linked to AIPL1: A mouse model reveals destabilization of cGMP phosphodiesterase
- L3 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Functional studies of AIPL1: potential role of AIPL1 in cell cycle exit and/or differentiation of photoreceptors
- L3 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The phenotype of Leber congenital amaurosis in patients with AIPL1 mutations
- L3 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Role of AIP and its homologue the blindness-associated protein AIPL1 in regulating client protein nuclear translocation
- L3 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Leber congenital amaurosis: Comprehensive survey of the genetic heterogeneity, refinement of the clinical definition, and genotype-phenotype correlations as a strategy for molecular diagnosis
- L3 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Abolished interaction of NUB1 with mutant AIPL1 involved in Leber congenital amaurosis
- L3 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Analysis of three genes in Leber congenital amaurosis in Indonesian patients
- L3 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI AIPL1, a protein implicated in Leber's congenital amaurosis, interacts with and aids in processing of farnesylated proteins
- L3 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Attenuation of the activity of the cAMP-specific phosphodiesterase PDE4A5 by interaction with the immunophilin XAP2

- L3 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Delineating the molecular basis of human genetic diseases: epigenetic and functional studies
- L3 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The inherited blindness associated protein AIPL1 interacts with the cell cycle regulator protein NUB1. [Erratum to document cited in CA138:118994]
- L3 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Mutation screening of Pakistani families with congenital eye disorders
- L3 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Mutations in the AIPL1 gene encoding an aryl receptor interacting protein homolog on chromosome 17p cause Leber congenital amaurosis 4
- L3 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Method of treating or retarding the development of blindness
- L3 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The inherited blindness associated protein AIPL1 interacts with the cell cycle regulator protein NUB1
- L3 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Functional analysis of AIPL1: A novel photoreceptor-pineal specific protein causing Leber congenital amaurosis and other retinopathies
- L3 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Molecular genetics of Leber congenital amaurosis
- L3 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI The Leber congenital amaurosis gene product AIPL1 is localized exclusively in rod photoreceptors of the adult human retina
- L3 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Comparative analysis of aryl-hydrocarbon receptor interacting protein-like 1 (Aip1l), a gene associated with inherited retinal disease in humans
- L3 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Molecular genetics and prospects for therapy of the inherited retinal dystrophies
- L3 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Prevalence of mutations causing retinitis pigmentosa and other inherited retinopathies
- L3 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Prevalence of AIPL1 Mutations in Inherited Retinal Degenerative Disease
- L3 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2006 ACS on STN
TI Mutations in a new photoreceptor-pineal gene on 17p cause Leber congenital amaurosis

=> e sohocki m?/au
E1 7 SOHOCKI M/AU
E2 99 SOHOCKI M M/AU

E3 0 --> SOHOCKI M?/AU
 E4 2 SOHOCKI MELANIE/AU
 E5 40 SOHOCKI MELANIE M/AU
 E6 1 SOHOCKI MELANIE MICHELLE/AU
 E7 2 SOHOCKI R/AU
 E8 1 SOHODA T/AU
 E9 2 SOHODE K/AU
 E10 1 SOHODE KANEYUKI/AU
 E11 1 SOHODLER A/AU
 E12 2 SOHOEL A/AU

=> el-e6
 L21 149 ("SOHOCKI M"/AU OR "SOHOCKI M M"/AU OR "SOHOCKI M?"/AU OR "SOHOCKI MELANIE"/AU OR "SOHOCKI MELANIE M"/AU OR "SOHOCKI MELANIE MICHELLE"/AU)

=> 13 not 121
 L22 180 L3 NOT L21

=> dup rem 13
 PROCESSING COMPLETED FOR L3
 L23 36 DUP REM L3 (0 DUPLICATES REMOVED)

=> dup rem 121
 PROCESSING COMPLETED FOR L21
 L24 64 DUP REM L21 (85 DUPLICATES REMOVED)

=> 123 not 124
 L25 33 L23 NOT L24

=> d ibib abs 125 1-33

L25 ANSWER 1 OF 33 CAPIUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006:769226 CAPIUS <<LOGINID::20060824>>
 TITLE: Detection of somatic mutation in blood in the early diagnosis of cancer
 INVENTOR(S): North, Don Adams
 PATENT ASSIGNEE(S): Sky Genetics, Inc., USA
 SOURCE: PCT Int. Appl., 92pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2006081248 | A2 | 20060803 | WO 2006-US2500 | 20060124 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| US 2006183893 | A1 | 20060817 | US 2005-311594 | 20051219 |
| PRIORITY APPLN. INFO.: | | | US 2005-646961P | P 20050125 |

US 2005-669639P P 20050408
US 2005-311594 A 20051219

AB A method of cancer diagnosis that involves detection of cancer-associated somatic mutations in peripheral blood is described. Cancer markers are most commonly mutated or abnormal DNA sequences associated with metastatic cancer. Markers may be detected using PCR, microarrays, or other nucleic acid or peptide-based assays. These methods may be used for a variety of diagnostic purposes, including initial, early-stage or later diagnosis of cancer, particularly metastatic cancer and monitoring of cancer or treatment progression. The cancer markers may also be used to create a cancer marker profile. Treatment may be directed based on this profile. Addnl., methods using blood may provide a cancer marker profile of mutations or abnormalities found in at least one of several tumors in the body, instead of merely one tumor. The invention also include kits, such as primer kits, and microarrays for use in performing the various methods.

L25 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:651349 CAPLUS <<LOGINID::20060824>>
TITLE: Exclusion of LCA5 locus in a consanguineous Turkish family with macular coloboma-type LCA
AUTHOR(S): Ozguel, R. K.; Bozkurt, B.; Kiratli, H.; Ogus, A.
CORPORATE SOURCE: Department of Molecular Biology, Hacettepe University, Ankara, Turk.
SOURCE: Eye (London, United Kingdom) (2006), 20(7), 817-819
CODEN: EYEEEC; ISSN: 0950-222X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Leber's congenital amaurosis (LCA) is an inherited retinal dystrophy, which causes severe visual impairment in early childhood. Recent mol. genetic studies have linked 11 loci (AIPL1, CRB1, CRX, GUCY2D, RPE65, RDH12, RPGRIP1, TULP1, LCA3, LCA5, and LCA9) to LCA. LCA5 is a new locus, which maps to the 6q11-q16 chromosomal region and was found to be associated with macular coloboma-type LCA in a Pakistani family. Herein, we describe the mol. genetic features of a consanguineous Turkish family in which four children have macular coloboma-type LCA. Methods: Haplotype anal. was performed on the DNA of the family members using microsatellite markers against GUCY2D, RPE65, and LCA5. Genomic DNA was screened for mutations by means of single-strand conformational polymorphism (SSCP) anal. in exons of the RPE65 and CRX genes. Results: In haplotype anal., no linkage to LCA5 or GUCY2D loci was detected. None of the tested markers showed homozygosity or segregation between affected siblings. PCR-SSCP mutation anal. revealed no mutations in the screened RPE65 and CRX genes. Conclusion: We excluded LCA5 as the genetic cause of macular coloboma-type LCA in this Turkish family. Macular coloboma-type LCA shows genetic heterogeneity and it is not possible to establish a phenotype-genotype correlation with LCA5 and macular coloboma.

L25 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:875831 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:264770
TITLE: Predominant rod photoreceptor degeneration in Leber congenital amaurosis
AUTHOR(S): van der Spuy, Jacqueline; Munro, Peter M. G.; Luthert, Philip J.; Preising, Markus N.; Bek, Toke; Heegaard, Steffen; Cheetham, Michael E.
CORPORATE SOURCE: Division of Pathology and Institute of Ophthalmology, University College London, London, UK
SOURCE: Molecular Vision (2005), 11, 542-553
CODEN: MVEPFB; ISSN: 1090-0535
URL: <http://www.molvis.org/molvis/v11/a64/v11a64-vander-spuy.pdf>

PUBLISHER: Molecular Vision
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB An unusual retinal vascular morphol. in an enucleated eye from a patient with Leber congenital amaurosis (LCA) has been associated with a mutation in AIPL1. The AIPL1 protein is expressed in the pineal gland and retinal photoreceptors. In the retina, AIPL1 is expressed in both developing cone and rod photoreceptors, but it is restricted to rod photoreceptors in the adult human retina. Therefore, this study was conducted to determine the photoreceptor phenotype in this LCA patient to determine if photoreceptors were differentially affected. Addnl. genetic screening was performed and the consequences of the H82Y amino acid substitution characterized in an in vitro assay of NUB1 modulation. The morphol. of the photoreceptors was examined by light and electron microscopy. Immunohistochem. and immunofluorescent confocal microscopy was performed using a range of retinal photoreceptor markers. Transfection of the H82Y mutant AIPL1 in SK-N-SH cells revealed a normal subcellular localization and solubility but resulted in an increased ability of AIPL1 to redistribute GFP-NUB1 to the cytoplasm and resolve NUB1 fragment inclusion formation. Morphol., the LCA retina appeared to be cone-dominant with a single layer of cone-like cells remaining in the central retina. Photoreceptor outer segments were absent and the surviving residual inner segments were severely shortened. Severe degeneration of the LCA retina was associated with upregulation of glial fibrillary acidic protein (GFAP). No signal was detected for AIPL1, rhodopsin, or L/M and S cone opsins in the LCA retina. Double labeling with peanut agglutinin (PNA) and wheat germ agglutinin (WGA) supported a cone-dominant phenotype for the surviving photoreceptors in the LCA retina, as did double labeling for cone arrestin, and rod and cone recoverin. The cone arrestin signal was restricted to the residual photoreceptor inner segments and was not detected in the cell bodies, axons, or axon terminals of the surviving photoreceptors. Recoverin immunoreactivity was most intense in the residual photoreceptor inner segments. The phenotype in this patient suggests that although AIPL1 is required for the development of normal rod and cone photoreceptor function, it might only be essential for rod and not cone survival in the adult.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:671727 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:166667
TITLE: The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs
INVENTOR(S): Ueno, Yuki; Tsuda, Takanori; Takanori, Hitoshi; Yoshikawa, Toshikazu; Osawa, Toshihiko
PATENT ASSIGNEE(S): Biomarker Science Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 85 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| JP 2005198640 | A2 | 20050728 | JP 2004-53258 | 20040227 |
| PRIORITY APPLN. INFO.: | | | JP 2003-394758 | A 20031125 |
| AB The curcuminoids- and anthocyanins-responsive gene expression profiles in adipocytes have been revealed. The curcuminoids- and anthocyanins- | | | | |

responsive genes are designed to be used as the index markers in the screenings of the substances that can affect the gene expression patterns in obesity and diabetes. These substances can be the candidates of anti-obesity and anti-diabetes drugs. Therefore, the groups of curcuminoids- and anthocyanins-responsive genes are intended to be used as markers in a form of kit such as DNA chip for the screening of anti-obesity and anti-diabetes drugs.

L25 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:420383 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:167734
TITLE: Dioxin: a review of its environmental effects and its aryl hydrocarbon receptor biology
AUTHOR(S): Mandal, Prabir K.
CORPORATE SOURCE: Department of Biology, University of North Florida, Jacksonville, FL, 32224, USA
SOURCE: Journal of Comparative Physiology, B: Biochemical, Systemic, and Environmental Physiology (2005), 175(4), 221-230
CODEN: JPBPD1; ISSN: 0174-1578
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. A highly persistent trace environmental contaminant and one of the most potent toxicants known is dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin or TCDD). TCDD induces a broad spectrum of biol. responses, including induction of cytochrome P 450 1A1 (CYP1A1), disruption of normal hormone signaling pathways, reproductive and developmental defects, immunotoxicity, liver damage, wasting syndrome, and cancer. Its classification was upgraded from "possible human carcinogen" (group 2B) to "human carcinogen" (group 1) by the International Agency for Research on Cancer (IARC) in 1997. Exposure to TCDD may also cause changes in sex ratio, and tumor promotion in other animals. Because of the growing public and scientific concern, toxicol. studies were initiated to analyze the short- and long-term effects of dioxin. TCDD brings about a wide variety of toxic and biochem. effects via aryl hydrocarbon receptor (AhR)-mediated signaling pathways. Essential steps in this adaptive mechanism include AhR binding of ligand in the cytoplasm of cells associated with 2 mols. of chaperone heatshock protein (Hsp90) and AhR interactive protein, translocation of the receptor to the nucleus, dimerization with the Ah receptor nuclear translocator, and binding of this heterodimeric transcription factor (present in CYP1A) to dioxin-responsive elements upstream of promoters that regulate the expression of genes involved in xenobiotic metabolism
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:265452 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 143:76091
TITLE: A missense mutation in GUCY2D acts as a genetic modifier in RPE65-related Leber congenital amaurosis
AUTHOR(S): Silva, Eduardo; Dharmaraj, Sharola; Li, Ying Ying; Pina, Ana Luisa; Carter, Robert Colin; Loyer, Magali; Traboulsi, Elias; Theodosiadis, George; Koenekoop, Robert K.; Sundin, Olof H.; Maumenee, Irene H.
CORPORATE SOURCE: Molecular and Developmental Biology Laboratory, Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: Ophthalmic Genetics (2004), 25(3), 205-217
CODEN: OGENEN; ISSN: 0167-6784
PUBLISHER: Taylor & Francis The Netherlands

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Leber congenital amaurosis (LCA) is a clin. and genetically heterogeneous severe retinal dystrophy presenting in infancy. To explain the phenotypical variability observed in two affected siblings of a consanguineous pedigree diagnosed with LCA and establish a genotype-phenotype correlation, we screened GUCY2D, RPE65, CRX, AIPL1, and RPGRIP1 for mutations. The more severely affected sibling carried a heterozygous missense mutation in the GUCY2D gene (Ile539Val), which did not segregate with the disease phenotype. Subsequently, a homozygous nonsense mutation (Glu102STOP) in the RPE65 gene was identified in both affected siblings, thus identifying the causative gene. This data provides evidence for the presence of genetic modulation in LCA. It appears that the heterozygous GUCY2D mutation further disrupts the already compromised. Photoreceptor function resulting in more severe retinal dysfunction in the older sibling. We suggest that the unusual phenotypic variability in these two siblings with LCA is caused by the modifying effect of a heterozygous GUCY2D mutation observed against the disease background of a homozygous RPE65 mutation.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:265442 CAPLUS <<LOGINID::20060824>>

DOCUMENT NUMBER: 143:75565

TITLE: Leber congenital amaurosis: A genetic paradigm

AUTHOR(S): Allikmets, Rando

CORPORATE SOURCE: Departments of Ophthalmology and Pathology, Columbia University, New York, NY, USA

SOURCE: Ophthalmic Genetics (2004), 25(2), 67-79

CODEN: OGENEN; ISSN: 0167-6784

PUBLISHER: Taylor & Francis The Netherlands

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Leber congenital amaurosis (LCA; estimated prevalence 1:50,000-100,000) is an early-onset inherited cause of childhood blindness characterized by a severe retinal dystrophy immediately after birth. Variants in at least six genes, AIPL1, CRB1, CRX, GUCY2D, RPE65, and RPGRIP1, have been associated with a diagnosis consistent with LCA or early-onset retinitis pigmentosa and together account for less than 50% of all LCA cases. Genetically heterogeneous inheritance has complicated the mol. anal. of LCA cases, especially sporadic ones where conventional methods

are

of limited value. Until recently, the management of patients with LCA relied mainly on clin. examination, electrophysiolog., and other ancillary tests. Genotyping, i.e., determining the exact genetic defect causing LCA in each specific case, was not routinely performed since the comprehensive screening of six genes by SSCP and/or direct sequencing is relatively inefficient and cost-prohibitive. Patients, therefore, were often left with no specific information on their disease status. Recent advances in genotyping technologies have allowed the introduction of comprehensive and affordable screening procedures to determine causal genetic variation, resulting in precise mol. diagnosis, more accurate visual prognosis, and suggestions towards treatment options.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:91096 CAPLUS <<LOGINID::20060824>>

DOCUMENT NUMBER: 143:384284

TITLE: AIPL1, the protein that is defective in

Leber congenital amaurosis, is essential for the

biosynthesis of retinal rod cGMP phosphodiesterase.
[Erratum to document cited in CA141:330028]
AUTHOR(S): Liu, Xiaoqing; Bulgakov, Oleg V.; Wen, Xiao-Hong;
Woodruff, Michael L.; Pawlyk, Basil; Yang, Jun; Fain,
Gordon L.; Sandberg, Michael A.; Makino, Clint L.; Li,
Tiansen
CORPORATE SOURCE: Berman-Gund Laboratory for the Study of Retinal
Degenerations, Harvard Medical School, Boston, MA,
02114, USA
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America (2005), 102(2), 515
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the ordinate label in Figure 5B, "r/rpeak" appeared incorrectly as "pA"; the corrected version of Figure 5 is given. This correction does not affect the conclusions of the article.

L25 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1047682 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 142:72707
TITLE: Retinal degeneration in Aipl1-deficient
mice: a new genetic model of Leber congenital
amaurosis
AUTHOR(S): Dyer, Michael A.; Donovan, Stacy L.; Zhang, Jiakun;
Gray, Jonathan; Ortiz, Angelica; Tenney, Rebeca; Kong,
Jian; Allikmets, Rando; Sohocki, Melanie M.
CORPORATE SOURCE: Department of Developmental Neurobiology, St. Jude
Children's Research Hospital, Memphis, TN, 38105, USA
SOURCE: Molecular Brain Research (2004), 132(2), 208-220
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is the most severe inherited retinopathy, with the earliest age of onset. Because this currently incurable disease is present from birth and is a relatively rare disorder, the development of animal models that closely resemble the phenotype in patients is especially important. The authors' previous genetic analyses of LCA patients identified mutations in the aryl-hydrocarbon interacting protein-like 1 (AIPL1) gene. Here they present the development of an animal model of AIPL1-associated LCA, the Aipl1-deficient mouse. Aipl1 is expressed at low levels throughout human and mouse retinal development and is rapidly upregulated as photoreceptors differentiate. The mouse displays rapid retinal degeneration and massive Mueller cell gliosis, resembling the phenotype of the rd mouse, which is caused by a mutation in the gene for the β -subunit of the rod-specific phosphodiesterase. The authors confirm that this phenotype is consistent with the human disease using electroretinograms, and document the disease pathogenesis by analyzing the development of all retinal cell types and synaptogenesis during retinal histogenesis. Ectopic expression of AIPL1 led to deregulated retinal progenitor cell proliferation and alterations in cell fate specification; however, no gross abnormalities of proliferation during retinal development were detected. Data from anal. of proliferation and cell fate specification during retinal development of Aipl1-deficient mice suggests that there may be redundancy or compensation for Aipl1 loss by other related proteins. Because this mouse model closely mimics the human retinopathy caused by homozygous mutations in this gene, it provides a preclin. model for testing therapies to rescue the vision of children whose blindness is caused by AIPL1 mutations.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:939432 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 142:4818
TITLE: The Leber Congenital Amaurosis Protein AIPL1
Modulates the Nuclear Translocation of NUB1 and
Suppresses Inclusion Formation by NUB1 Fragments
AUTHOR(S): van der Spuy, Jacqueline; Cheetham, Michael E.
CORPORATE SOURCE: Institute of Ophthalmology, Division of Pathology,
University College London, London, EC1V 9EL, UK
SOURCE: Journal of Biological Chemistry (2004), 279(46),
48038-48047
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations in the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) cause the blinding disease Leber congenital amaurosis (LCA). The similarity of AIPL1 to AIP has led to suggestions that AIPL1 could function in a similar manner to AIP in facilitating protein translocation and as a component of chaperone complexes. AIPL1 interacts with the cell cycle regulator NEDD8 ultimate buster protein 1 (NUB1). As AIPL1 is predominantly cytoplasmic and NUB1 is predominantly nuclear, the authors tested the hypothesis that AIPL1 could modulate the nuclear translocation of NUB1. Co-transfection of AIPL1 with GFP-NUB1 resulted in a shift of GFP-NUB1 subcellular distribution toward the cytoplasm. Interestingly, AIPL1 was able to act in a chaperone-like fashion to efficiently suppress inclusion formation by NUB1 fragments. Co-transfection of AIPL1 with GFP-NUB1-N and GFP-NUB1-C resulted in an AIPL1-dependent suppression of GFP-NUB1-N perinuclear inclusions and GFP-NUB1-C intranuclear inclusions leading to the redistribution of these fragments in the cytoplasm. This chaperone-like function of AIPL1 was specific for NUB1, since AIPL1 was unable to suppress the inclusion formation by unrelated aggregation-prone proteins and AIP had no effect on NUB1 localization or inclusion formation. The authors examined the effect of a range of pathogenic and engineered mutations on the ability of AIPL1 to modulate NUB1 localization or inclusion formation. With the exception of W278X, which formed nonfunctional SDS-insol. inclusions, all of the pathogenic mutations studied were soluble and could modulate NUB1 with varying efficiency compared with the wild-type protein. The effect of AIPL1 on NUB1 required the C-terminal region of AIPL1, as engineered C-terminal truncation mutations had no effect on NUB1. These data show that AIPL1 can modulate protein translocation and act in a chaperone-like manner and suggest that AIPL1 is an important modulator of NUB1 cellular function.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:829150 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 141:347987
TITLE: Purification, characterization and intracellular localization of aryl hydrocarbon interacting protein-like 1 (AIPL1) and effects of mutations associated with inherited retinal dystrophies
AUTHOR(S): Gallon, Victoria A.; Wilkie, Susan E.; Deery, Evelyn

C.; Newbold, Richard J.; Sohocki, Melanie M.; Bhattacharya, Shomi S.; Hunt, David M.; Warren, Martin J.

CORPORATE SOURCE: School of Biological Sciences, Queen Mary, University of London, London, E1 4NS, UK

SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (2004), 1690(2), 141-149
CODEN: BBADEX; ISSN: 0925-4439

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mutations in AIPL1 are associated with Leber Congenital Amaurosis (LCA), a major cause of childhood blindness, yet the cellular function of the encoded protein has yet to be fully elucidated. In order to investigate the biochem. of AIPL1, we have developed a system for the expression of the recombinant protein in bacteria and its subsequent purification. The secondary structure and thermostability of wild-type and mutant proteins have been examined by CD (CD) spectroscopy. Some of the variants, notably W278X and P376S, had markedly different secondary structure compns., indicating that the proteins had not folded properly, while W278X and T114I were particularly thermolabile. When eukaryotic cells were transfected with the AIPL1 expression constructs, we show by immunofluorescence microscopy that wild-type protein is distributed throughout the nucleus and cytoplasm. Several of the mutants give similar results. With two of the disease-associated variants (W278X and A336Δ2), however, the protein remains in the cytoplasm in aggresome-like particles. These particles were shown to be ubiquitinated, indicating that the mutant protein had been tagged for proteasomal degradation. On this basis, we can conclude that wild-type protein is expressed in a soluble and folded manner, and that some of the disease-associated mutant proteins are nonfunctional because they are insol. and are degraded by the cell. Other mutations appear to have a more localized effect on secondary structure, which does not result in insol. or affect protein targeting, but reduces the stability of the protein at human body temperature.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:817749 CAPLUS <>LOGINID::20060824>>

DOCUMENT NUMBER: 141:289104

TITLE: Use of adeno-associated virus serotype 4 in mediating transduction of retinal pigmented epithelium of mammals after subretinal delivery

INVENTOR(S): Rolling, Fabienne; Weber, Michel

PATENT ASSIGNEE(S): Universite de Nantes, Fr.

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004084951 | A2 | 20041007 | WO 2004-EP4020 | 20040326 |
| WO 2004084951 | A3 | 20041118 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, | | | | |

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

US 2004208847 A1 20041021 US 2003-400531 20030328

PRIORITY APPLN. INFO.: US 2003-400531 A 20030328

AB The present invention provides use of adeno-associated virus serotype 4 in mediating transduction of retinal pigmented epithelium of mammals after subretinal delivery. AAV-4 capsid protein is administered to a primate. In particular, the invention relates to means and methods for preventing, treating or alleviating an eye disease in a mammal.

L25 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:808381 CAPLUS <<LOGINID::20060824>>

DOCUMENT NUMBER: 141:330028

TITLE: AIPL1, the protein that is defective in

Leber congenital amaurosis, is essential for the

biosynthesis of retinal rod cGMP phosphodiesterase

Liu, Xiaoqing; Bulgakov, Oleg V.; Wen, Xiao-Hong;
Woodruff, Michael L.; Pawlyk, Basil; Yang, Jun; Fain,
Gordon L.; Sandberg, Michael A.; Makino, Clint L.; Li,
Tiansen

CORPORATE SOURCE: Berman-Gund Laboratory for the Study of Retinal
Degenerations, Harvard Medical School, Boston, MA,
02114, USA

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America (2004), 101(38), 13903-13908
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) is a member of the FK-506-binding protein family expressed specifically in retinal photoreceptors. Mutations in AIPL1 cause Leber congenital amaurosis, a severe early-onset retinopathy that leads to visual impairment in infants. Here the authors show that knockdown of AIPL1 expression in mice also produces a retinopathy but over a more extended time course. Before any noticeable pathol., there was a reduction in the level of rod cGMP phosphodiesterase (PDE) proportional to the decrease in AIPL1 expression, whereas other photoreceptor proteins were unaffected. Consistent with less PDE in rods, flash responses had a delayed onset, a reduced gain, and a slower recovery of flash responses. The authors suggest that AIPL1 is a specialized chaperone required for rod PDE biosynthesis. Thus loss of AIPL1 would result in a condition that phenocopies retinal degenerations in the rd mouse and in a subgroup of human patients.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:808380 CAPLUS <<LOGINID::20060824>>

DOCUMENT NUMBER: 141:330027

TITLE: Leber congenital amaurosis linked to AIPL1:

A mouse model reveals destabilization of cGMP phosphodiesterase

AUTHOR(S): Ramamurthy, Visvanathan; Niemi, Gregory A.; Reh,
Thomas A.; Hurley, James B.

CORPORATE SOURCE: Department of Biochemistry, University of Washington,
Seattle, WA, 98195, USA

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (2004), 101(38), 13897-13902
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA4) has been linked to mutations in the photoreceptor-specific gene Aryl hydrocarbon interacting protein like 1 (Aip1l). To investigate the essential role of AIPL1 in retina, the authors generated a mouse model of LCA by inactivating the Aip1l gene. In Aip1l-/- retinas, the outer nuclear layer develops normally, but rods and cones then quickly degenerate. Aip1l-/- mice have highly disorganized, short, fragmented photoreceptor outer segments and lack both rod and cone electroretinogram responses. Recent biochem. evidence indicates that AIPL1 can enhance protein farnesylation. The authors' study reveals that rod cGMP phosphodiesterase, a farnesylated protein, is absent and cGMP levels are elevated in AIPL1-/- retinas before the onset of degeneration. The authors' findings demonstrate that AIPL1 enhances the stability of phosphodiesterase and is essential for photoreceptor viability.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:647291 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 142:275624
TITLE: Functional studies of AIPL1: potential role of AIPL1 in cell cycle exit and/or differentiation of photoreceptors
AUTHOR(S): Akey, Dayna T.; Zhu, Xuemei; Dyer, Michael; Li, Amin; Sorensen, Adam; Fukada-Kamitani, Taeko; Daiger, Stephen P.; Craft, Cheryl; Kamitani, Tetsu; Sohocki, Melanie M.
CORPORATE SOURCE: University of Cincinnati, Cincinnati, OH, 45267, USA
SOURCE: Advances in Experimental Medicine and Biology (2003), 533(Retinal Degenerations), 287-295
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aryl hydrocarbon receptor interacting protein-like 1 (AIPL1) plays a role in cytosolic stability and/or nuclear transport of NUB1 during regulation of cell cycle progression during photoreceptor development. This function would be consistent with the severe, early-onset blindness observed in patients with Leber congenital amaurosis caused by mutations of AIPL1. It was shown that co-immunopptn. expts. in cells of retinal origin that AIPL1 specifically interacts with a 50 kDa NUB1 protein, which is 16 kDa smaller than that present in other tissues.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:639867 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 141:258623
TITLE: The phenotype of Leber congenital amaurosis in patients with AIPL1 mutations
AUTHOR(S): Dharmaraj, Sharola; Leroy, Bart P.; Sohocki, Melanie M.; Koenekoop, Robert K.; Perrault, Isabelle; Anwar, Khalid; Khaliq, Shagufta; Devi, R. Summathi; Birch, David G.; de Pool, Elaine; Izquierdo, Natalio; van Maldergem, Lionel; Ismail, Mohammad; Payne, Annette

CORPORATE SOURCE: M.; Holder, Graham E.; Bhattacharya, Shomi S.; Bird, Alan C.; Kaplan, Josseline; Maumenee, Irene H.
Johns Hopkins Center for Hereditary Eye Diseases,
Baltimore, MD, USA

SOURCE: Archives of Ophthalmology (Chicago, IL, United States)
(2004), 122(7), 1029-1037
CODEN: AROPAW; ISSN: 0003-9950

PUBLISHER: American Medical Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Studies were carried out to describe the phenotype of Leber congenital amaurosis (LCA) in 26 probands with mutations in aryl hydrocarbon receptor interacting protein-like 1 protein (AIPL1) and compare it with phenotypes of other LCA-related genes and to describe the electroretinogram (ERG) in heterozygote carriers. Patients with AIPL1-related LCA were identified in a cohort of 303 patients with LCA by polymerase chain reaction single-strand confirmational polymorphism mutation screening and/or direct sequencing. Phenotypic characterization included clin. and ERG evaluation. Seven heterozygous carrier parents also underwent ERG testing. Seventeen homozygotes and 9 compound heterozygotes were identified. The W278X mutation was most frequent (48% of alleles). Visual acuities ranged from light perception to 20/400. Variable retinal appearances, ranging from near normal to varying degrees of chorioretinal atrophy and intraretinal pigment migration, were noted. Atrophic and/or pigmentary macular changes were present in 16 (80%) of 20 probands. Keratoconus and cataracts were identified in 5 (26%) of 19 patients, all of whom were homozygotes. The ERG of a parent heterozygote carrier revealed significantly reduced rod function, while ERGS for 6 other carrier parents were normal. Thus, the phenotype of LCA in patients with AIPL1 mutations is relatively severe, with a maculopathy in most patients and keratoconus and cataract in a large subset. Rod ERG abnormalities may be present in heterozygous carriers of AIPL1 mutations. Understanding and recognizing the phenotype of LCA may help in defining the course and severity of the disease. Identifying the gene defect is the first step in preparation for therapy since mol. diagnosis in LCA will mandate the choice of treatment.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:615045 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 141:240738

TITLE: Role of AIP and its homologue the blindness-associated protein AIPL1 in regulating client protein nuclear translocation

AUTHOR(S): van der Spuy, J.; Cheetham, M. E.

CORPORATE SOURCE: Division of Pathology, Institute of Ophthalmology, University College London, London, EC1V 9EL, UK

SOURCE: Biochemical Society Transactions (2004), 32(4), 643-645
CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mutations in the AIPL1 (aryl hydrocarbon receptor interacting protein-like 1) cause the blinding disease Leber's congenital amaurosis. AIPL1 is a homolog of the AIP. AIP functions as part of a chaperone heterocomplex to facilitate signaling by the AhR and plays an important role in regulating the nuclear translocation of the receptor. We review the evidence for the role of AIP in protein translocation and compare the potential functions of AIPL1 in the translocation of its interacting partner the NEDD8 ultimate buster

protein 1.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:375810 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 141:121675
TITLE: Leber congenital amaurosis: Comprehensive survey of the genetic heterogeneity, refinement of the clinical definition, and genotype-phenotype correlations as a strategy for molecular diagnosis
AUTHOR(S): Hanein, Sylvain; Perrault, Isabelle; Gerber, Sylvie; Tanguy, Gaelle; Barbet, Fabienne; Ducrocq, Dominique; Calvas, Patrick; Dollfus, Helene; Hamel, Christian; Lopponen, Tuija; Munier, Francis; Santos, Louisa; Shalev, Stavit; Zafeiriou, Dimitrios; Dufier, Jean-Louis; Munnich, Arnold; Rozet, Jean-Michel; Kaplan, Josseline
CORPORATE SOURCE: Unite de Recherches sur les Handicaps Genetiques de l'Enfant, Hopital Necker - Enfants Malades, Paris, Fr.
SOURCE: Human Mutation (2004), 23(4), 306-317
CODEN: HUMUE3; ISSN: 1059-7794
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is the earliest and most severe form of all inherited retinal dystrophies, responsible for congenital blindness. Disease-associated mutations have been hitherto reported in seven genes. These genes are all expressed preferentially in the photoreceptor cells or the retinal pigment epithelium but they are involved in strikingly different physiol. pathways resulting in an unforeseeable physiopathol. variety. This wide genetic and physiol. heterogeneity that could largely increase in the coming years, hinders the mol. diagnosis in LCA patients. The genotyping is, however, required to establish genetically defined subgroups of patients ready for therapy. Here, the authors report a comprehensive mutational anal. of the all known genes in 179 unrelated LCA patients, including 52 familial and 127 sporadic (27/127 consanguineous) cases. Mutations were identified in 47.5% patients. GUCY2D appeared to account for most LCA cases of our series (21.2%), followed by CRB1 (10%), RPE65 (6.1%), RPGRIP1 (4.5%), AIPL1 (3.4%), TULP1 (1.7%), and CRX (0.6%). The clin. history of all patients with mutations was carefully revisited to search for phenotype variations. Sound genotype-phenotype correlations were found that allowed patients to be divided into two main groups. The first one includes patients whose symptoms fit the traditional definition of LCA, i.e., congenital or very early cone-rod dystrophy, while the second group gathers patients affected with severe yet progressive rod-cone dystrophy. Besides, objective ophthalmol. data allowed each group to be subdivided into two subtypes. Based on these findings, the authors have drawn decisional flowcharts directing the mol. anal. of LCA genes in a given case. These flowcharts will hopefully lighten the heavy task of genotyping new patients but only if one has access to the most precise clin. history since birth.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:309237 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 140:337231
TITLE: Abolished interaction of NUB1 with mutant AIPL1 involved in Leber congenital amaurosis
AUTHOR(S): Kanaya, Koichi; Sohocki, Melanie M.; Kamitani, Tetsu
CORPORATE SOURCE: Medical School, Department of Internal Medicine, The

SOURCE: University of Texas-Houston Health Science Center,
Houston, TX, 77030, USA
Biochemical and Biophysical Research Communications
(2004), 317(3), 768-773
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is often considered the most severe inherited retinopathy, and AIPL1 was the fourth gene identified as associated with LCA. Although the function of AIPL1 is unknown, it has been reported to interact with NUB1. Here, the authors searched for a NUB1-binding site on AIPL1 and located it between amino acid residues 181 and 330 in AIPL1. Importantly, many LCA-associated mutations of AIPL1 have been found at this site. Hence, the authors hypothesized that the interaction between NUB1 and AIPL1 is affected in patients with LCA. To test this possibility, the authors used three different assays to investigate the interaction between NUB1 and the AIPL1 mutants associated with LCA. Some of the AIPL1 mutants did not interact with NUB1, suggesting that abolishment of this interaction is involved in the pathogenesis of LCA. Other AIPL1 mutants, however, did interact with NUB1, suggesting that other mols. are also involved in the pathogenesis.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:881235 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 140:161686
TITLE: Analysis of three genes in Leber congenital amaurosis in Indonesian patients
AUTHOR(S): Sitorus, Rita S.; Lorenz, Birgit; Preising, Markus N.
CORPORATE SOURCE: Department of Paediatric Ophthalmology, Strabismology and Ophthalmogenetics, klinikum, University of Regensburg, Regensburg, 93053, Germany
SOURCE: Vision Research (2003), 43(28), 3087-3093
CODEN: VISRAM; ISSN: 0042-6989
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose. To assess the frequency, the pattern of disease causing mutations, and phenotypic variations in patients with Leber congenital amaurosis (LCA) from Indonesia. Patients and methods. Twenty-one unrelated index cases with a clin. diagnosis of LCA were screened for mutations in the coding sequence of RetGC1, RPE65 and AIPL1 gene with single strand conformation polymorphism anal. followed by direct sequencing and restriction enzyme digestion. Results. Four novel disease causing mutations were identified: Three in the RPE65 gene (106del9bp, G32V and Y435C) in two of 21 index cases and one in the AIPL1 (K14E). Two of them were homozygous and one was compound-heterozygous. No disease causing mutation was identified in RetGC1. Conclusions. The four novel disease causing mutations identified in this study confirmed the diagnosis of LCA which has not been recognized before in Indonesia. The frequency of RPE65 mutations was 9.5%; and of AIPL1 mutations 4.8%. This was in general accordance with previous studies reported from other countries. Unlike in those studies, no disease causing RetGC1 mutations could be identified in the authors' patients. Phenotypically, the RPE65 and AIPL1 mutations identified in this study caused nearly total blindness by the second decade of life, but had a different onset of symptoms. The patients with the RPE65 mutations retained some useful visual function until the end of the first decade, which progressed to total blindness during the second decade of life, whereas the

(homozygous) AIPL1 mutation was associated with nearly total blindness from infancy on. Therefore, RPE65 mutations have to be considered to cause early onset severe retinal degeneration (EOSRD), and AIPL1 mutations a form of LCA.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:876446 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 139:362949
TITLE: AIPL1, a protein implicated in Leber's congenital amaurosis, interacts with and aids in processing of farnesylated proteins
AUTHOR(S): Ramamurthy, Visvanathan; Roberts, Melanie; van den Akker, Focco; Niemi, Gregory; Reh, T. A.; Hurley, James B.
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(22), 12630-12635
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The most common form of blindness at birth, Leber's congenital amaurosis (LCA), is inherited in an autosomal recessive fashion. Mutations in six different retina-specific genes, including a recently discovered gene, AIPL1, have been linked to LCA in humans. To understand the mol. basis of LCA caused by aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) mutations, and to elucidate the normal function of AIPL1, we performed a yeast two-hybrid screen using AIPL1 as bait. The screen demonstrated that AIPL1 interacts specifically with farnesylated proteins. Mutations in AIPL1 linked to LCA compromise this activity. These findings suggest that the essential function of AIPL1 within photoreceptors requires interactions with farnesylated proteins. Anal. of isoprenylation in cultured human cells shows that AIPL1 enhances the processing of farnesylated proteins. Based on these findings, we propose that AIPL1 interacts with farnesylated proteins and plays an essential role in processing of farnesylated proteins in retina.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:662645 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 139:303706
TITLE: Attenuation of the activity of the cAMP-specific phosphodiesterase PDE4A5 by interaction with the immunophilin XAP2
AUTHOR(S): Bolger, Graeme B.; Peden, Alexander H.; Steele, Michael R.; MacKenzie, Carolyn; McEwan, David G.; Wallace, Derek A.; Huston, Elaine; Baillie, George S.; Houslay, Miles D.
CORPORATE SOURCE: Departments of Medicine (Division of Oncology) and Oncological Science, Huntsman Cancer Institute, Veterans Affairs Medical Center, University of Utah Health Sciences Center, Salt Lake City, UT, 84148, USA
SOURCE: Journal of Biological Chemistry (2003), 278(35), 33351-33363
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The cAMP-specific phosphodiesterase (PDE4) isoform PDE4A5 interacted with the immunophilin XAP2 in a yeast two-hybrid assay. The interaction was confirmed in biochem. pull-down analyses. The interaction was specific, in that PDE4A5 did not interact with the closely related immunophilins AIPL1, FKBP51, or FKBP52. XAP2 also did not interact with other PDE4A isoforms or typical isoforms from the three other PDE4 subfamilies. Functionally, XAP2 reversibly inhibited the enzymic activity of PDE4A5, increased the sensitivity of PDE4A5 to inhibition by the prototypical PDE4 inhibitor 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-pyrrolidinone (rolipram) and attenuated the ability of cAMP-dependent protein kinase to phosphorylate PDE4A5 in intact cells. XAP2 maximally inhibited PDE4A5 by .apprx.60%, with an IC₅₀ of 120 nM, and reduced the IC₅₀ for rolipram from 390 nM to 70-90 nM. Co-expression of XAP2 and PDE4A5 in COS7 cells showed that they could be co-immunopptd. and also reduced both the enzymic activity of PDE4A5 and its IC₅₀ for rolipram. Native XAP2 and PDE4A5 could be co-immunopptd. from the brain. The isolated COOH-terminal half of XAP2 (amino acids 170-330), containing its tetratricopeptide repeat domain, but not the isolated NH₂-terminal half (amino acids 1-169), containing the immunophilin homol. region, similarly reduced PDE4A5 activity and its IC₅₀ for rolipram. Mutation of Arg271 to alanine, in the XAP2 tetratricopeptide repeat region, attenuated its ability to both interact with PDE4A5 in two-hybrid assays and to inhibit PDE4A5 activity. Either the deletion of a specific portion of the unique amino-terminal region or specific mutations in the regulatory UCR2 domain of PDE4A5 attenuated its ability be inhibited by XAP2. We suggest that XAP2 functionally interacts with PDE4A5 in cells.

REFERENCE COUNT:

59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:650597 CAPLUS <>LOGINID::20060824>>

DOCUMENT NUMBER: 140:26532

TITLE: Delineating the molecular basis of human genetic diseases: epigenetic and functional studies

AUTHOR(S): Akey, Dayna Tirpak

CORPORATE SOURCE: Health Science Center, Univ. of Texas, Houston, TX, USA

SOURCE: (2002) 179 pp. Avail.: UMI, Order No. DA3070963
From: Diss. Abstr. Int., B 2003, 63(11), 5033

DOCUMENT TYPE: Dissertation

LANGUAGE: English

AB Unavailable

L25 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:83959 CAPLUS <>LOGINID::20060824>>

DOCUMENT NUMBER: 138:318985

TITLE: Mutation screening of Pakistani families with congenital eye disorders

AUTHOR(S): Khaliq, Shagufta; Abid, Aiysha; Hameed, Abdul; Anwar, Khalid; Mohyuddin, Aisha; Azmat, Zobia; Shami, S. A.; Ismail, Muhammad; Mehdi, S. Qasim

CORPORATE SOURCE: Dr A. Q. Khan Research Laboratories, Biomedical and Genetic Engineering Division, Islamabad, Pak.

SOURCE: Experimental Eye Research (2003), 76(3), 343-348
CODEN: EXERA6; ISSN: 0014-4835

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To map the disease loci several Pakistani families suffering from autosomal recessive retinitis pigmentosa with preserved para-arteriolar

retinal pigment epithelium and Leber congenital amaurosis (LCA) were analyzed. Anal. revealed close genetic linkage between the disease phenotype of some of the families (3330RP, 111RP and 010LCA) and the microsatellite markers on chromosome 1q31. Mutation screening of the candidate gene CRB1 revealed a G to A transversion in exon 7 in arRP family 330RP and a T to C substitution in another arRP family, 111RP. In exon 9 of the CRB1 gene a T to C transversion was found in the family suffering from LCA (010LCA). The LCA phenotype of another family (011LCA) in which the CRB1 locus was excluded, showed linkage with microsatellite markers D17S1294 and D17S796 on chromosome 17p13.1. The association of the candidate gene GUCY2D (17p13.1) with the disease phenotype was excluded as no disease-associated mutation was found in any of its exons. Mutation screening of another candidate gene, AIPL1 located in the same region, showed a novel homozygous C to A substitution in exon 2. These sequence changes are unique for the Pakistani families and some of these have not been reported previously.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:813853 CAPLUS <<LOGINID::20060824>>
 DOCUMENT NUMBER: 137:289058
 TITLE: Method of treating or retarding the development of blindness
 INVENTOR(S): Acland, Gregory M.; Aguirre, Gustavo D.; Bennett, Jean; Hauswirth, William W.; Maguire, Albert M.; Jacobson, Samuel G.
 PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA; The University of Florida; Cornell Research Foundation, Inc.
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002082904 | A2 | 20021024 | WO 2002-US11314 | 20020411 |
| WO 2002082904 | A3 | 20021219 | | |
| W: AU, CA, JP, NZ, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| CA 2442670 | AA | 20021024 | CA 2002-2442670 | 20020411 |
| EP 1381276 | A2 | 20040121 | EP 2002-725607 | 20020411 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| US 2004022766 | A1 | 20040205 | US 2002-300720 | 20021120 |
| PRIORITY APPLN. INFO.: | | | US 2001-283766P | P 20010413 |
| | | | WO 2002-US11314 | W 20020411 |

AB A method for treating an ocular disorder characterized by the defect or absence of a normal gene in the ocular cells of a human or animal subject involves administering to the subject by subretinal injection an effective amount of a recombinant adeno-associated virus carrying a nucleic acid sequence encoding the normal gene under the control of a promoter sequence which expresses the product of the gene in the ocular cells. The ocular cells are preferably retinal pigment epithelial (RPE) cells, and the gene is preferably an RPE-specific gene, e.g., <i>RPE65</i>. The promoter is one that can express the gene product in the RPE cells. Compns. for subretinal administration are useful in this method.

L25 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:800037 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 138:118994
TITLE: The inherited blindness associated protein
AIPL1 interacts with the cell cycle regulator
protein NUB1
AUTHOR(S): Akey, Dayna T.; Zhu, Xuemei; Dyer, Michael; Li, Aimin;
Sorensen, Adam; Blackshaw, Seth; Fukuda-Kamitani,
Taeko; Daiger, Stephen P.; Craft, Cheryl M.; Kamitani,
Tetsu; Sohocki, Melanie M.
CORPORATE SOURCE: Department of Environmental Health, Center for Genome
Information, University of Cincinnati, Cincinnati, OH,
45267, USA
SOURCE: Human Molecular Genetics (2002), 11(22), 2723-2733
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations in the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) gene have been found in patients with Leber congenital amaurosis (LCA), a severe, early-onset form of retinal degeneration. To determine the normal function of AIPL1 and to better understand how mutations in this gene cause disease, we performed a yeast two-hybrid screen to identify bovine and human retinal AIPL1-interacting proteins. One of the identified interacting proteins corresponds to NUB1 (NEDD8 Ultimate Buster 1), which is thought to control many biol. events, especially cell cycle progression, by down-regulating NEDD8 expression. The human AIPL1-NUB1 interaction was verified by co-immunopptn. studies in Y79 retinoblastoma cells, demonstrating that this interaction occurs within cells that share a number of features with retinal progenitor cells. Furthermore, we examined the localization of the human AIPL1 protein within developing and adult retinas, and found that AIPL1 is present in the developing photoreceptor layer of the human retina and within the photoreceptors of the adult retina. Similar to AIPL1, NUB1 is also expressed in the developing and adult retina. Therefore, it is possible that the early-onset form of retinal degeneration seen in LCA patients with AIPL1 mutations may be due to a defect in the regulation of cell cycle progression during photoreceptor maturation. These data raise the possibility that AIPL1 is important for appropriate photoreceptor formation during development and/or survival following differentiation.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:418792 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 138:301211
TITLE: Molecular genetics of Leber congenital amaurosis
AUTHOR(S): Cremers, Frans P. M.; van den Hurk, Jose A. J. M.; den Hollander, Anneke I.
CORPORATE SOURCE: Department of Human Genetics, University Medical Center Nijmegen, Nijmegen, 6500 HB, Neth.
SOURCE: Human Molecular Genetics (2002), 11(10), 1169-1176
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. Leber congenital amaurosis (LCA) is the most common inherited cause of blindness in childhood and is characterized by a severe retinal dystrophy before the age of one year. Six genes have been identified that together account for approx. half of all LCA patients. These genes are expressed preferentially in the retina or the retinal

pigment epithelium. Their putative functions are quite diverse and include retinal embryonic development (CRX), photoreceptor cell structure (CRB1), phototransduction (GUCY2D), protein trafficking (AIPL1, RPGRIP1), and vitamin A metabolism (RPE65). The mol. data for CRB1 and RPE65 support previous hypotheses that LCA can represent the severe end of a spectrum of retinal dystrophies. Given the diverse mechanisms underlying the disease, future therapies of LCA may need to be tailored to certain genetically defined subgroups. Based on exptl. evidence in mice and dogs, patients with disturbed retinal metabolism of vitamin A through a mutation in the RPE65 gene will likely be the first candidates for future therapeutic trials.

REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:325840 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 137:165134
TITLE: The Leber congenital amaurosis gene product AIPL1 is localized exclusively in rod photoreceptors of the adult human retina
AUTHOR(S): Van der Spuy, Jacqueline; Chapple, J. Paul; Clark, Brian J.; Luthert, Philip J.; Sethi, Charanjit S.; Cheetham, Michael E.
CORPORATE SOURCE: Department of Pathology, Institute of Ophthalmology, University College London, London, EC1V 9EL, UK
SOURCE: Human Molecular Genetics (2002), 11(7), 823-831
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA) is the most severe inherited retinal dystrophy resulting in markedly impaired vision or blindness at birth. LCA is characterized by an extinguished electroretinogram in infancy, which is thought to be indicative of an early and severe impairment of both the rod and cone photoreceptors in the human retina. Recently, the aryl hydrocarbon receptor-interacting protein-like 1 (AIPL1) gene was identified as the fourth causative gene of LCA. AIPL1 encodes a 384 amino acid protein of unknown function. We have generated a polyclonal antibody against a peptide from a unique region within the primate AIPL1 protein, which detects a protein of .apprx.43 kDa in human retinal exts. A screen of human tissues and immortalized cell lines with this antibody reveals AIPL1 to be specific to human retina and cell lines of retinal origin (Y79 retinoblastoma cells). Within the retina, AIPL1 was detected only in the rod photoreceptor cells of the peripheral and central human retina. The AIPL1 staining pattern extended within the rod photoreceptor cells from the inner segments, through the rod nuclei to the rod photoreceptor synaptic spherules in the outer plexiform layer. AIPL1 was not detected in the cone photoreceptors of peripheral or central human retina. This study is the first to suggest that AIPL1 performs a function essential to the maintenance of rod photoreceptor function.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:462017 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 136:195781
TITLE: Comparative analysis of aryl-hydrocarbon receptor interacting protein-like 1 (Aipl1), a gene associated with inherited retinal disease in humans
AUTHOR(S): Sohocki, Melanie M.; Sullivan, Lori S.; Tirpak, Dayna L.; Daiger, Stephen P.

CORPORATE SOURCE: Human Genetics Center, School of Public Health,
Houston, TX, 77225-0334, USA
SOURCE: Mammalian Genome (2001), 12(7), 566-568
CODEN: MAMGEC; ISSN: 0938-8990
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations in AIPL1 cause Leber congenital amaurosis (LCA), the most severe form of inherited blindness in children; however, the function of this protein in normal vision remains unknown. To determine amino acid subsequences likely to be important for function, we have compared the protein sequence of several species. Sequence conservation is highest across the three Aip1l tetratricopeptide (TPR) motifs and extends across the protein, except for a proline-rich amino acid sequence present only at the C-terminus of primate Aip1l. The length of the proline-rich region varies within primates; however, the length differences between human and primate Aip1l do not correlate with evolutionary distance. These observations reinforce the importance of the TPR domains for function, the similarity of Aip1l to a family of proteins that act as mol. chaperones, and the importance of comparative sequencing data for determination of whether AIPL1 sequence variants in patients are likely to cause retinopathy.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:418098 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 135:150635
TITLE: Molecular genetics and prospects for therapy of the inherited retinal dystrophies
AUTHOR(S): Bessant, David A. R.; Ali, Robin R.; Bhattacharya, Shomi S.
CORPORATE SOURCE: Department of Molecular Genetics, Institute of Ophthalmology, University College London, London, EC1V 9EL, UK
SOURCE: Current Opinion in Genetics & Development (2001), 11(3), 307-316
CODEN: COGDET; ISSN: 0959-437X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 69 refs. More than 60 genes responsible for human retinal dystrophies have been identified. Those recently isolated include the transcription factor genes NRL and NR2E3, RDH5 (retinol dehydrogenase), EFEMP1 (which encodes an extracellular matrix protein), CRB1, PROML1, RP1, AIPL1 and USH1C (harmonin). The ABCR protein has been identified as a critical transporter in the recycling of retinal (vitamin A). At present, a number of novel therapeutic strategies are being evaluated including pharmacol. treatments, cell transplantation and gene therapy. The progress made with such approaches now offers hope to patients with these incurable forms of blindness.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:75816 CAPLUS <<LOGINID::20060824>>
DOCUMENT NUMBER: 135:32249
TITLE: Prevalence of mutations causing retinitis pigmentosa and other inherited retinopathies
AUTHOR(S): Sohocki, Melanie M.; Daiger, Stephen P.; Bowne, Sara J.; Rodriguez, Joseph A.; Northrup, Hope; Heckenlively, John R.; Birch, David G.; Mintz-Hittner,

CORPORATE SOURCE: Helen; Ruiz, Richard S.; Lewis, Richard A.; Saperstein, David A.; Sullivan, Lori S.
Human Genetics Center, University of Texas-Houston Health Science Center, Houston, TX, 77225-0334, USA
SOURCE: Human Mutation (2001), 17(1), 42-51
CODEN: HUMUE3; ISSN: 1059-7794
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Inherited retinopathies are a genetically and phenotypically heterogeneous group of diseases affecting approx. one in 2000 individuals worldwide. For the past 10 yr, the Laboratory for Mol. Diagnosis of Inherited Eye Diseases (LMDIED) at the University of Texas-Houston Health Science Center has screened subjects ascertained in the United States and Canada for mutations in genes causing dominant and recessive autosomal retinopathies. A combination of single strand conformational anal. (SSCA) and direct sequencing of five genes (rhodopsin, peripherin/RDS, RPL1, CRX, and AIPL1) identified the disease-causing mutation in approx. one-third of subjects with autosomal dominant retinitis pigmentosa (adRP) or with autosomal dominant cone-rod dystrophy (adCORD). In addition, the causative mutation was identified in 15% of subjects with Leber congenital amaurosis (LCA). Overall, the authors report identification of the causative mutation in 105 of 506 (21%) of unrelated subjects (probands) tested; the authors report five previously unreported mutations in rhodopsin, two in peripherin/RDS, and one previously unreported mutation in the cone-rod homeobox gene, CRX. Based on this large survey, the prevalence of disease-causing mutations in each of these genes within specific disease categories is estimated. These data are useful in estimating the frequency of specific mutations and in selecting individuals and families for mutation-specific studies.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:426345 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 133:206257
TITLE: Prevalence of AIPL1 Mutations in Inherited Retinal Degenerative Disease
AUTHOR(S): Schock, Melanie M.; Perrault, Isabelle; Leroy, Bart P.; Payne, Annette M.; Dharmaraj, Sharola; Bhattacharya, Shomi S.; Kaplan, Josseline; Maumenee, Irene H.; Koenekoop, Robert; Meire, Francoise M.; Birch, David G.; Heckenlively, John R.; Daiger, Stephen P.
CORPORATE SOURCE: Human Genetics Center, School of Public Health, University of Texas-Houston Health Science Center, Houston, TX, 77225-0334, USA
SOURCE: Molecular Genetics and Metabolism (2000), 70(2), 142-150
CODEN: MGMEFF; ISSN: 1096-7192
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leber congenital amaurosis (LCA) is the most severe form of inherited retinal dystrophy and the most frequent cause of inherited blindness in children. LCA is usually inherited in an autosomal recessive fashion, although rare dominant cases have been reported. One form of LCA, LCA4, maps to chromosome 17p13 and is genetically distinct from other forms of LCA. The authors recently identified the gene associated with LCA4, AIPL1 (aryl-hydrocarbon interacting protein-like 1) and identified 3 mutations that were the cause of blindness in 5 families with LCA. In

this study, AIPL1 was screened for mutations in 512 unrelated probands with a range of retinal degenerative diseases to determine if AIPL1 mutations cause other forms of inherited retinal degeneration and to determine the relative contribution of AIPL1 mutations to inherited retinal disorders in populations worldwide. The authors identified 11 LCA families whose retinal disorder is caused by homozygous or compound heterozygous AIPL1 mutations. The authors also identified affected individuals in 2 apparently dominant families, diagnosed with juvenile retinitis pigmentosa or dominant cone-rod dystrophy, resp., who are heterozygous for a 12-bp AIPL1 deletion. The authors' results suggest that AIPL1 mutations cause approx. 7% of LCA worldwide and may cause dominant retinopathy. (c) 2000 Academic Press.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:46362 CAPLUS <>LOGINID::20060824>>
DOCUMENT NUMBER: 132:192794
TITLE: Mutations in a new photoreceptor-pineal gene on 17p cause Leber congenital amaurosis
AUTHOR(S): Sohocki, Melanie M.; Bowne, Sara J.; Sullivan, Lori S.; Blackshaw, Seth; Cepko, Constance L.; Payne, Annette M.; Bhattacharya, Shomi S.; Khaliq, Shagufta; Mehdi, S. Qasim; Birch, David G.; Harrison, Wilbur R.; Elder, Frederick F. B.; Heckenlively, John R.; Daiger, Stephen P.
CORPORATE SOURCE: Human Genetics Center, School of Public Health, The University of Texas-Houston Health Science Center, Houston, TX, USA
SOURCE: Nature Genetics (2000), 24(1), 79-83
CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leber congenital amaurosis (LCA, MIM 204000) accounts for at least 5% of all inherited retinal disease and is the most severe inherited retinopathy with the earliest age of onset. Individuals affected with LCA are diagnosed at birth or in the first few months of life with severely impaired vision or blindness, nystagmus and an abnormal or flat electroretinogram (ERG). Mutations in GUCY2D, RPE65 and CRX are known to cause LCA, but one study identified disease-causing GUCY2D mutations in only 8 of 15 families whose LCA locus maps to 17p13.1, suggesting another LCA locus might be located on 17p13.1. Confirming this prediction, the LCA in one Pakistani family mapped to 17p13.1, between D17S849 and D17S960 - a region that excludes GUCY2D. The LCA in this family has been designated LCA4. The authors describe here a new photoreceptor/pineal-expressed gene, AIPL1 (encoding aryl-hydrocarbon interacting protein-like 1), that maps within the LCA4 candidate region and whose protein contains three tetra-tripeptide (TPR) motifs, consistent with nuclear transport or chaperone activity. A homozygous nonsense mutation at codon 278 is present in all affected members of the original LCA4 family. AIPL1 mutations may cause approx. 20% of recessive LCA, as disease-causing mutations were identified in 3 of 14 LCA families not tested previously for linkage.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1 FILE 'REGISTRY' ENTERED AT 18:56:18 ON 24 AUG 2006
 L1 2 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L2 FILE 'CAPLUS' ENTERED AT 18:57:29 ON 24 AUG 2006
 L2 2 L1
 L3 36 AIP1

L4 FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
 L4 18:58:27 ON 24 AUG 2006
 L4 268 AIP1
 L5 77 ARYL (S) HYDROCARBON (S) RECEPTOR (S) INTERACTING (S) PROTEIN (

L6 69 L4 AND L5
 L7 276 L4 OR L5
 L8 6 TRP278X AND L7
 L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

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L10 FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
 L10 19:15:47 ON 24 AUG 2006
 L10 33 DUP REM L6 (36 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
 19:15:59 ON 24 AUG 2006

FILE 'STNGUIDE' ENTERED AT 19:21:06 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
 19:35:29 ON 24 AUG 2006
 L11 243 L7 NOT L10
 L12 184 PY>2001 AND L11
 L13 59 L11 NOT L12
 L14 27 DUP REM L13 (32 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 19:40:29 ON 24 AUG 2006

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
 19:45:05 ON 24 AUG 2006
 L15 242 L3 NOT L14
 L16 0 L3 NOT L4
 L17 242 L3 NOT L14
 L18 6 TRP? AND L17
 L19 2 L18 NOT L8

L20 2 DUP REM L19 (0 DUPLICATES REMOVED)
E SOHOCKI M?/AU
L21 149 E1-E6
L22 180 L3 NOT L21
L23 36 DUP REM L3 (0 DUPLICATES REMOVED)
L24 64 DUP REM L21 (85 DUPLICATES REMOVED)
L25 33 L23 NOT L24

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NEWS 9 JUN 02 The first reclassification of IPC codes now complete in
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NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced
NEWS 13 JUL 14 FSTA enhanced with Japanese patents
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI
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